New research areas inspired by sustainable development

Eric da Silva, Wissam Dayoub, Nicolas Duguet, Estelle Métay, Florence Popowycz, Marc Lemaire

► To cite this version:

Eric da Silva, Wissam Dayoub, Nicolas Duguet, Estelle Métay, Florence Popowycz, et al.. New research areas inspired by sustainable development. *Comptes Rendus. Chimie*, 2013, 16 (4), pp.343-349. 10.1016/j.crci.2012.12.019 . hal-01178718

HAL Id: hal-01178718

<https://hal.science/hal-01178718>

Submitted on 3 Jun 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

NEW RESEARCH AREAS INSPIRED BY SUSTAINABLE DEVELOPMENT

Eric Da Silva,^a Wissam Dayoub,^a Nicolas Duguet,^a Estelle Métay,^a Florence Popowycz^b and Marc Lemaire^{a*}

^a*Laboratoire de Catalyse, Synthèse et Environnement, Institut de Chimie et de Biochimie Moléculaires et Supramoléculaires ICBMS-CNRS-UMR 5246, Université Claude Bernard – Lyon 1, Bâtiment Curien 43, boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex, France*

^b*Laboratoire de Chimie Organique et Bio-organique, Institut National des Sciences Appliquées (INSA-Lyon), ICBMS-CNRS-UMR 5246, Bâtiment Jules Verne, 1^{er} étage, 20 Avenue Albert Einstein 69621 Villeurbanne Cedex*

*Corresponding author: E-Mail : marc.lemaire.chimie@univ-lyon1.fr; tel: (+33) (0)4 72 43 14 07; fax: (+33) (0)4 72 43 14 08

ABSTRACT

More than twenty years after its birth, Green Chemistry is definitely entered in its golden age. In this account, we highlight some of our progress made over the last ten years towards the development of green methodologies. We investigated various aspects of green chemistry such as new reagents, catalysts, transformations and solvents and also the utilization of renewable resources. We report herein four mature projects illustrating our efforts in these fields: i) polyhydrosiloxanes as new reducing agents, ii) glycerol as new platform for amphiphilic molecules, iii) water, room-temperature ionic liquids and supercritical carbon dioxide as new solvents, iv) C(sp²)-H activation as new C-C bond formation methodology. An overview of each project is given and the potential applications are discussed.

(Key-words: Green Chemistry, polyhydrosiloxanes, glycerol, scCO₂, C(sp²)-H activation).

INTRODUCTION

Waste minimization has always been a consideration since the beginning of industrial chemistry. As early as the 19th century, Ernest Solvay depicted a clean process for the production of sodium carbonate that generates only water and calcium chloride as ultimate by-products, thus ending the polluting “Leblanc process”. If this discovery had been made today, it would have been surely called « Green Chemistry ». Since the term has been coined by Paul Anastas in 1991 and the twelve principles have been erected as guidelines for its development, this concept has emerged as a new field on its own, having now its own scientific community, peer-reviewed journals, specialized meetings and so on. The main reason for this fast-growing interest is not only the awareness of sustainable development but also the fact that it provides new challenges for both academic and industrial researchers. One striking example is the preparation of 2,5-furandicarboxylic acid (2,5-FDCA) from renewable resources. This product has recently drawn a lot of attention for the potential replacement of phthalates in polymers such as polyesters or polyamides. The production of FDCA is in the focus of many chemical industries but is also of great interest from a fundamental point of view; new, cleaner and safer methodologies should be developed in order to render its access as green as possible.

In our laboratory, green methodologies have been developed for several years, keeping in mind that they should be amenable to large-scale and easily transferable to industry. That is why, in most of the

cases, our projects were conducted in collaboration with industrial partners. These partnerships led us to explore many different aspects of green chemistry, such as the development of new cleaner and safer reagents, catalysts, transformations and solvents and the utilization of renewable resources as feedstock. Herein, we illustrate each facet with a mature project: i) new reduction methodologies using polyhydrosiloxanes for the replacement of boron and aluminum hydrides, ii) valorization of glycerol through reductive alkylation with aldehydes or acids, iii) use of water, ionic liquids or supercritical carbon dioxide as low-environmental impact solvents, iv) C(sp²)-H activation methodologies as alternatives to classic cross-coupling reactions.

1. New reagents: Reduction with TMDS for the substitution of classic hydrides

Nowadays, it is necessary to design and elaborate new processes and reagents in order to reduce or eliminate the safety risks (both for operators and production chains) linked to the utilization of hazardous substances. The reduction of different functions (amide, ketone, aldehyde or ester) can be performed with high selectivity and efficiency with boron and aluminum hydrides. These reducers produced at 2000-3000 t/year and widely used in industry are dangerous partly due to their extreme reactivity with water.¹ They are often used in excess and reactions are usually performed in water-soluble solvents.² Treatment of such reactions is often complex due to the large production of salts which are potentially toxic^{3,4,5} and present in large quantities. An alternative to these technologies is the development of silicon hydrides associated to organometallic complexes.⁶ Indeed the ultimate waste of silicon derivatives is inert. Among silicon hydrides, hydrosilanes have been known to selectively reduce organic functions depending on the nature of the associated metal. However, even if the results are highly interesting in term of efficiency and selectivity, there remain some risks to exploit these compounds notably due to their toxicity and their flammability. Moreover, some of them (HSi(OEt)₃ or HSiCl₃), in the presence of a transition metal, can generate, *via* a redistribution reaction, a highly pyrophoric gas (SiH₄). These drawbacks can explain the limitation to the development of these methodologies in large scale.⁷ On the other side, polyhydrosiloxanes, which are relatively cheap and stable (in air and water), can also be used for the reduction of organic functions even in industry. Polymethylhydrosiloxane (PMHS) is typically a colourless liquid that is soluble in most organic solvents and inert towards air and moisture.⁸ PMHS which is prepared from cyclic siloxanes, is commercially available and has shown promising results for the reduction of organic functions, in some cases with good enantioselectivity. Amongst polyhydrosiloxanes, TMDS or tetramethyldisiloxane offers several benefits in comparison with PMHS. Notably the formation of a gel during the reaction was never observed with TMDS and the quantity of hydride is usually close to the stoichiometry. TMDS is issued from silicon industry and the by-product obtained at the end of the reaction can be employed as a water-repellent treatment of materials. Nevertheless, until now, it was less explored.^{9,10,11} With the collaboration of two industrial partners, we have previously reported the utilization of TMDS for the reduction of a large variety of organic functions. The initial study was dedicated to the reduction of phosphine oxides (Scheme 1). The reduction of secondary and tertiary phosphine oxides has been performed in the presence of TMDS and Ti(OPr)₄. Mechanistic studies have shown the formation of a Ti^{III}/Ti^{IV} cluster which could be the active species.¹² The same metallic complex with TMDS can

[illegible]

All methodologies developed in the laboratory used polyhydrosiloxanes with a quantity of hydrides close to the stoichiometry (number of hydrides in comparison with the function to be reduced). This consideration is important from an economic point of view as well as for security reasons. The nature of the used solvent such as methylcyclohexane and methyltetrahydrofuran has a low environmental impact because they are not hydrosoluble. Metals with low toxicity like titanium and iron have been favored and utilized in catalytic quantities. The work-up of the reaction only needs a small quantity of water to hydrolyze titanium complexes. This hydrolysis step is not exothermic, contrary to the treatment of reaction using aluminum or boron hydride.

“Biodiesel”, *i.e.* fatty acid methyl esters, has been widely implemented in the EU and the US since it has proved to be a valuable fuel for diesel engines, being both renewable and clean.^{20,21} It is obtained from vegetable oils (soybean, rapeseed ...) by a transesterification process with alcohols. The sharp rise in world biodiesel production has created a glut of glycerol, which is a by-product of the transesterification process. Today, its production is estimated to 2.6 million metric tons against 1.0 million metric tons in 2005 thus resulting in lower prices for this raw material. Therefore, the sustainability of this branch requires the development of new markets. In our laboratory, we have been

interested in the synthesis of glycerol derivatives, especially of non-symmetrical 1-O-alkyl glycerol ethers. These compounds are amphiphilic molecules used as performance additives in various industrial fields (textiles, leather, metallurgy ...) and are also present in the formulations of end-user products such as detergents, cosmetics, industrial cleaning...²² Non-symmetrical 1-O-alkyl glycerol ethers belong to the family of non-ionic surfactants that are very popular because of their low irritancy and their high stability in acidic medium. Traditionally, these ethers are prepared *via* the Williamson ether synthesis, despite the need for a strong base and the generation of stoichiometric amounts of saline waste.²³ Moreover, the few procedures that are reported in the literature for the synthesis of ethers implementing catalysts (nickel on silica, platinum oxide, acid catalysis ...), give only low yields. More than 15 years ago, our group discovered an alternative method to the Williamson etherification of carbonyl compounds with linear alcohols using Pd/C as a catalyst under hydrogen pressure.²⁴ This method allows the synthesis of ethers with high yields and generates water as the sole by-product. However, to the best of our knowledge, this method has never been applied to polyols in mild conditions. The few examples reported are patents that describe two step-procedures, at high pressures and temperatures.²⁵ This long-underexploited reaction was recently trendy with the increased interest for glycerol chemistry that allowed us to find a real application in cooperation with a major industry in the French sector of vegetable oils / proteins and a leader company in specialty chemicals. The application of this reaction to glycerol was realized through the use of 1 mol% of Pd/C, 10 bar of H₂ pressure, and a Brønsted acid as a co-catalyst at 140°C. Under these conditions, the reaction of an aldehyde or a ketone with glycerol afforded the corresponding 1-O-alkyl glycerol ethers (Scheme 2) with both high yields and selectivity.²⁶ Same products can also be obtained from carboxylic acid and glycerol. In this case, the reaction was realized at 120°C under 50 bar of H₂ pressure in the presence of 1 mol% of Pd/C and a solid acid co-catalyst (Amberlyst A35).²⁷ After 16 hours of reaction, the catalyst is filtered off and the product separated from the medium by a liquid-liquid extraction. These two methodologies have also been extended to larger polyols such as diglycerol.

Scheme 2. Access to 1-O-alkyl glycerol ethers

In conclusion, we have developed a straightforward and mild eco-friendly process for the synthesis of 1-alkyl mono- and di-glycerol ethers with both high yield and selectivity as well as no production of undesired inorganic salts but water as the only stoichiometric by-product. This highly selective process opens a new alternative to the Williamson etherification for the synthesis of linear 1-O-alkyl (di)glycerol ethers with modular hydrophilic-lipophilic balances, that are of great interest in many research fields.

3. New solvents: Water, RTIL and scCO₂ as a new alternative to common organic solvents

Water is currently considered as the best solvent for organic synthesis but presents some limitations and drawbacks for organic and organometallic chemistry. Due to its high polarity, its use in the presence of apolar molecules is much reduced in industrial and academic research. Therefore, organic solvents are intensively used in industrial chemical processes and extremely efficient in term of reactivity. However, organic solvents have tendency to be flammable, highly volatile, expensive and toxic (carcinogenic, mutagenic and reprotoxic). From a scientific point of view, the green chemistry concepts (principles 5 and 12) force the use of new alternatives and make them compatible with sustainable development. During the last decade, new solvents coming up to societal expectances and regulations have been developed. There are intensive efforts to make novative reactions and processes based on ionic liquids, supercritical fluids (such as carbon dioxide with critical point at $P_c = 74$ bar and $T_c = 31^\circ\text{C}$) and fluorinated derivatives as new solvent s. Through various examples published by our group, the use of afore mentioned solvents as media for catalyzed reactions or processes for treatment, separation or recycling has been reported. The first example deals with the selective extraction of polar nitrogen compounds (toward sulfur compounds) from hydrocarbon feed using liquid/liquid extraction using chloride based ionic liquids (imidazolium and pyridinium ions).²⁸ The enantioselective hydrogenation of β -cetoester has been studied in the presence of polar ammonium BINAP catalyst and room temperature ionic liquids (RTILs). The results have shown similar conversion and yield in comparison with those observed in the presence of water as a solvent (*Scheme 3*).²⁹ The synthesis of fluorinated ligands for asymmetric hydrogenation catalyzed by ruthenium has been performed in supercritical medium. Acetamidoacrylate has been reduced in apolar and homogeneous system due to the high affinity of fluorinated systems for carbon dioxide.³⁰

Scheme 3. Asymmetric catalytic hydrogenation in RTILs, water and scCO₂.

In a recent study, we have demonstrated the formation of glycol carbonate in supercritical condition where scCO_2 has been used as both solvent and chemical reagent.³¹ It is probably one of the most interesting routes in terms of synthetic method and atom economy (*Scheme 4*). Our efforts are now focused on the synthesis of new solvents from natural resources.

Scheme 4. Direct carbonatation of glycol derivatives under scCO_2 .

4. New transformations: Carbon-Carbon bond formation by $\text{C}(\text{sp}^2)\text{-H}$ activation. An alternative to metallo-catalyzed cross coupling reactions.

Aryl-aryl bond formation is one of the most important tools of modern organic synthesis, due to their large representation in natural products, pharmaceutical, agrochemical, material and polymer specialties.³² The direct arylation to promote the direct functionalization of the $\text{C}(\text{sp}^2)\text{-H}$ bond has received great attention from the chemistry community with an increasing number of recent publications related to the extension of the methodology to miscellaneous studies, mechanistic investigations as well as computational studies.³³ From on a synthetic point of view, this reaction can be considered as an efficient alternative to well-known metallo-catalyzed cross-coupling reactions (Kumada-Corriu, Suzuki, Sonogashira, Stille, Negishi).³⁴ These synthetic and methodological tools have been widely used in an impressive number of multi-step or total syntheses, requiring the former preparation of organometallic species as precursors (magnesium, boron, tin and zinc derivatives). In the case of the direct arylation, the metallic part of the molecule is replaced by an hydrogen, avoiding the costly preparation of these highly functionalized precursors (*Scheme 5*). This supplementary synthetic step avoided represents a significant saving in terms of solvent, purification, time, waste,...

Classic metallo-catalyzed cross-coupling reactions:

Direct Arylation:

Scheme 5. Metallo-catalyzed cross coupling reactions vs direct arylation

Recent reviews about C-H activation were recently published with an overview of the last twenty years of efforts.³⁵ The direct arylation is a promising synthetic methodology. In particular, regarding the environmental guideline requirements of green and sustainable chemistry, the methodology of direct arylation fits perfectly with three principles: atom economy (principle 2); reduction of derivatives / synthetic intermediates (principle 8); catalysis (principle 9).³⁶ During the last fifteen years, our group has been involved in this reaction concerning the functionalization of a wide range of heterocyclic systems, regarded as main building blocks in major pharmaceutical industries

due to their important biological / therapeutical properties.³⁷ The first example reported in the group was discovered with direct arylation of thiophene, focusing on the discovery of a new polymerization process for the preparation of polyalkylated thiophenes. The classic syntheses using iron^{III} in excess or Grignard reagents represent a serious restriction to an industrial development of these new materials. Activated thiophenes at C(2) position were subjected to coupling in the presence of aryl halide, tetrabutylammonium bromide, potassium carbonate and palladium acetate in a mixture acetonitrile / water (9/1) (Scheme 6). This ligandless procedure led to increased yields on C(2) substituted thiophenes in comparison with C(3) substituted thiophenes. The nature and the position of the substituent strongly influence the outcome of this reaction.³⁸

Scheme 6. Direct arylation of thiophene 2-carbonitrile

The procedure was next extended to benzo[*b*]thiophenes substituted in C(3) position, providing a new synthetic route to 2-arylbenzo[*b*]thiophenes.³⁹ More recently, new direction was investigated promoting the fruitful expertise gained in methodology to target molecules of high therapeutic interest. The application of direct arylation to numerous heterocyclic systems offers the opportunity to design novative alkaline phosphatases (to address osteoarthritis),⁴⁰ NorA pump (antibacterial agent)⁴¹ or heat shock protein 90 inhibitors (anti-cancer agent).⁴² Rhodamines displaying excellent photophysical properties have been also prepared following this strategy (Figure 1).⁴³

Figure 1. Direct arylation implemented to bioactive molecules

This new methodology, aiming to improve the atom economy and contribute to the sustainable development, led finally to a great ability to create more original structures with high impact on biological targets (both on enzymes as well as on receptors).

5. Conclusion

In conclusion, we have reported here four long-term programs illustrating our efforts to develop green and sustainable methodologies. First, we have shown that TMDS, in association with a metallic catalyst, could be a usable alternative to boron and aluminum hydrides. This reagent usually gives good chemio- and regio-selectivities and could be employed for a large panel of reduction reactions. Moreover, it is intrinsically safer than other hydrides, more stable to air, water and moisture and gives harmless by-products that could be valorized. We hope that further development will tend to decrease its price that is currently higher than classic boron and aluminum derivatives. Then, we have shown that glycerol or diglycerol could be valorized through a mild reductive alkylation reaction using aldehydes or carboxylic acids as alkylating agents. This clean transformation allows the preparation of amphiphilic compounds that could be potentially used as non-ionic surfactants. Large-scale preparation of such compounds and study of their physical properties are now under progress. In a third project, we have described the use of ionic liquids, water and supercritical carbon dioxide as alternatives to classical solvents for asymmetric hydrogenation using hydrogen as clean reductant. The preparation and the utilization of adequate chiral ligands have permitted to reach high levels of enantioselectivity (up to 95% in water). The use of supercritical carbon dioxide was further extended to the direct carbonatation of glycol derivatives to give the corresponding carbonates, opening new routes for the transformation of such compounds. Finally, we have demonstrated that green methodologies could also be developed within the frame of bioactive molecules. Direct arylation of activated thiophenes and benzothiophenes gave the corresponding substituted heterocycles with good yields and good atom-economies. This method was applied to the preparation of alkaline phosphatases, NorA pump, Hsp 90 inhibitors and to fluorescent rhodamines. The future will be definitely oriented towards sustainable chemistry and one step beyond towards Green chemical engineering. This contribution pointed out some academic efforts correlated to green chemistry.

---

¹ Li, J. J.; Johnson, D. S.; Sliskovic, D. R.; Roth, B. D. *Contemporary Drug Synthesis*, Wiley-Interscience; On line edition (Nov 11 2004).

² Spencer P. J. *Toxicol. Lett.* **2005**, 156, 181.

³ Report ECBI/132/04 Rev. 2-22 november 2004 <http://ecb.jrc.it/>

⁴ a) Sakamoto, T.; Saito, H.; Ishii, K.; Takahashi, H.; Tanabe, S.; Ogasawara, Y. *FEBS Letters* **2006**, 580, 6543; b) Banks, W. A.; Niehoff, M. L.; Drago, D.; Zatta, P. *Brain Res.* **2006**, 1116, 215.

⁵ Xu, Y.; Jiang, J.-Q. *Ind. Eng. Chem. Res.* **2008**, 47, 16.

-
- ⁶ (a) Larson, G. L.; Fry, J. L. Ionic and organometallic-catalyzed organosilane reductions, John Wiley & Sons, Inc., Hoboken, New Jersey, **2010**, 265; (b) Addis, D.; Das, S.; Junge, K.; Beller, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 6004.
- ⁷ Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1993**, *58*, 3221.
- ⁸ Lawrence, N. J.; Drew, M. D.; Bushell, S. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3381.
- ⁹ Lecea, B.; Aizpurua, J. M.; Palomo, C. *Tetrahedron Lett.* **1985**, *26*, 4657.
- ¹⁰ Lipshutz, B. H.; Shimizu, H. *Angew. Chem. Int. Ed.* **2004**, *43*, 2228.
- ¹¹ Nadkarni, D. V.; Hallissey, J. F. *Org. Process Res. Dev.* **2008**, *12*, 1142.
- ¹² a) Petit, C.; Favre-Régouillon, A.; Albela, B.; Bonnevot, L.; Mignani, G.; Lemaire, M. *Organometallics* **2009**, *28*, 6379; b) Petit, C.; Favre-Régouillon, A.; Mignani, G.; Lemaire, M. *Green Chem.* **2010**, *12*, 326.
- ¹³ a) Laval, S.; Dayoub, W.; Favre-Régouillon, A.; Berthod, M.; Demonchaux, P.; Mignani, G.; Lemaire, M. *Tetrahedron Lett.* **2009**, *50*, 7005; b) Laval, S.; Dayoub, W.; Favre-Régouillon, A.; Demonchaux, P.; Mignani, G.; Lemaire, M. *Tetrahedron Lett.* **2010**, *51*, 2092.
- ¹⁴ (a) Pehlivan, L.; Métay, E.; Laval, S.; Dayoub, W.; Demonchaux, P.; Mignani, G.; Lemaire, M. *Tetrahedron Lett.* **2010**, *51*, 1939. (b) Pehlivan, L.; Métay, E.; Laval, S.; Dayoub, W.; Demonchaux, P.; Mignani, G.; Lemaire, M. *Tetrahedron* **2011**, *67*, 1971.
- ¹⁵ Pehlivan, L.; Métay, E.; Boyron, O.; Demonchaux, P.; Mignani, G.; Lemaire, M. *Eur. J. Org. Chem.* **2011**, *24*, 4687.
- ¹⁶ Shi, Y.; Dayoub, W.; Chen, G.-R.; Lemaire, M. *Tetrahedron Lett.*, **2011**, *52*, 1281.
- ¹⁷ (a) Zhang, Y.-J.; Dayoub, W.; Chen, G.-R.; Lemaire, M. *Eur. J. Org. Chem.* **2012**, *10*, 1960; (b) Zhang, Y.-J.; Dayoub, W.; Chen, G.-R.; Lemaire, M. *Tetrahedron*, **2012**, *68*, 7400.
- ¹⁸ Pehlivan, L.; Métay, E.; Delbrayelle, D.; Mignani, G.; Lemaire, M. *Eur. J. Org. Chem.* **2011**, *36*, 7400.
- ¹⁹ (a) Pehlivan, L.; Metay, E.; Delbrayelle, D.; Mignani, G.; Lemaire, M. *Eur. J. Org. Chem.* **2012**, 4689-4693; (b) Pehlivan, L.; Metay, E.; Delbrayelle, D.; Mignani, G.; Lemaire, M. *Tetrahedron* **2012**, *68*, 3151-3155.
- ²⁰ Wilson, E. K. *Chem. Eng. News*, **2002**, *80*, 46.
- ²¹ Bagley, S. T.; Gratz, L. D.; Johnson, J. H.; McDonald, J. F. *Environ. Sci. Technol.*, **1998**, *32*, 1183.
- ²² (a) Shoji, N.; Yuikina, Y. 1994, EP N° 0624563. Kao corporation; (b) Arredondo, V. M.; Back, D. J.; Corrigan, P. J.; Kreuzer, D. P.; Cearley, A. C. WO 2007/113776 (2006). Procter & Gamble Company.
- ²³ Queste, S.; Baudin, P.; Touraud, D.; Kunz, W.; Aubry, J.-M. *Green Chem.* **2006**, *8*, 822.
- ²⁴ Bethmont, V.; Fache, F.; Lemaire, M. *Tetrahedron Lett.* **1995**, *36*, 4235.
- ²⁵ (a) Nakagawa, S.; Tottorinaka, H.-S. 1994, EP N° 0624563A1; (b) Nagasawa, A.; Okutsu, M.; Kitsuki, T. 2001, WO2001032306.
- ²⁶ (a) Shi, Y.; Dayoub, W.; Chen, G.-R.; Lemaire, M. *Green Chem.* **2010**, *12*, 2189. (b) Shi, Y.; Dayoub, W.; Chen, G.-R.; Lemaire, M. *Science China Chem.* **2010**, *53*, 1953. (c) Shi, Y.; Dayoub, W.; Favre-Régouillon, A.; Chen, G.-R.; Lemaire, M. *Tetrahedron Lett.* **2009**, *50*, 6891.
- ²⁷ Sutter, M.; Dayoub, W.; Métay, E.; Raoul, Y.; Lemaire, M. *ChemSusChem* **2012**, *5*, 1.

- ²⁸ Xie, L. L.; Favre-Réguillon, A.; Pellet-Rostaing, S.; Wang, X.-X.; Fu, X.; Estager, J.; Vrinat, M.; Lemaire, M. *Ind. Eng. Chem. Res.*, **2008**, *47*, 8801.
- ²⁹ Berthod, M.; Joerger, J.-M.; Mignani, G.; Vaultier, M.; Lemaire, M. *Tetrahedron : Asymmetry* **2004**, *15*, 2219.
- ³⁰ Berthod, M.; Mignani, G.; Lemaire, M. *Tetrahedron : Asymmetry*, **2004**, *15*, 1121.
- ³¹ (a) Da Silva, E.; Dayoub, W.; Mignani, G.; Raoul, Y.; Lemaire, M. *Catal. Commun.* **2012**, *29*, 58 ;
b) Da Silva, E.; Dayoub, W.; Mignani, G.; Raoul, Y.; Lemaire, M. PCT Patent WO 2012/095435 A1
- ³² Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.
- ³³ a) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447; b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792; c) Bellina, F.; Rossi, R. *Chem. Rev.* **2010**, *110*, 1082; d) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269; e) Thansandote, P.; Lautens, M. *Chem. Eur. J.* **2009**, *15*, 5874; f) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173.
- ³⁴ a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467; b) Negishi, E. I.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821; c) Tamao, K.; Kodama, S.; Nakajima, I.; Kumada, M.; Minato, A.; Suzuki, K. *Tetrahedron* **1982**, *38*, 3347; d) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374; e) Corriu, R. J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144a.
- ³⁵ a) McGlacken, G. P.; Bateman, L. M.; *Chem. Soc. Rev.* **2009**, *38*, 2447; b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792; c) Bellina, F.; Rossi, R. *Chem. Rev.* **2010**, *110*, 1082; d) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269; e) Thansandote, P.; Lautens, M. *Chem. Eur. J.* **2009**, *15*, 5874 ; f) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173.
- ³⁶ a) Anastas, P. T.; Warner, J. C. *Green chemistry: theory and practice*, Oxford University Press, New York, **1998**, 30; b) Tundo, P.; Anastas, P.; Black, D. StC.; Breen, J.; Collins, T.; Memoli, S.; Miyamoto, J.; Polyakoff, M.; Tumas, W. *Pure Appl. Chem.* **2000**, *72*, 1207.
- ³⁷ Popowycz, F.; Métay, E.; Lemaire, M. *C. R. Chimie* **2010**, *14*, 621.
- ³⁸ a) Gozzi, C.; Lavenot, L.; Ilg, K.; Penalva, V.; Lemaire, M. *Tetrahedron Lett.* **1997**, *38*, 8867 ; b) Lavenot, L.; Gozzi, C.; Ilg, K.; Orlova, I.; Penalva, V.; Lemaire, M. *J. Organomet. Chem.* **1998**, *567*, 49; c) Penalva, V.; Lavenot, L.; Gozzi, C.; Lemaire, M. *Appl. Catal. A* **1999**, *182*, 399; d) Sévignon, M.; Papillon, J.; Schulz, E.; Lemaire, M. *Tetrahedron Lett.* **1999**, *40*, 5873; e) Hassan, J.; Gozzi, C.; Schulz, E.; Lemaire, M. *J. Organomet. Chem.* **2003**, *687*, 280.
- ³⁹ a) Fournier Dit Chabert, J.; Gozzi, C.; Lemaire, M. *Tetrahedron Lett.* **2002**, *43*, 1829; b) Fournier Dit Chabert, J.; Joucla, L.; David, E.; Lemaire, M. *Tetrahedron* **2004**, *60*, 3221; c) David, E.; Perrin, J.; Pellet-Rostaing, S.; Fournier Dit Chabert, J.; Lemaire, M. *J. Org. Chem.* **2005**, *70*, 3569; d) Fournier Dit Chabert, J.; Chatelain, G.; Pellet-Rostaing, S.; Bouchu, D.; Lemaire, M. *Tetrahedron Lett.* **2006**, *47*, 1015 ; e) Liger, F.; Pellet-Rostaing, S.; Popowycz, F.; Lemaire, M. *Tetrahedron Lett.* **2011**, *52*, 3736.
- ⁴⁰ Li, L.; Chang, L.; Pellet-Rostaing, S.; Liger, F.; Lemaire, M.; Buchet, R.; Wu, Y. *Bioorg. Med. Chem.* **2009**, *17*, 7290.
- ⁴¹ Fournier Dit Chabert, J.; Marquez, B.; Neville, L.; Joucla, L.; Broussous, S.; Bouhours, P.; David, E.; Pellet-Rostaing, S.; Marquet, B.; Moreau, N.; Lemaire, M. *Bioorg. Med. Chem.* **2007**, *15*, 4482.

-
- ⁴² a) Gracia, S.; Cazorla, C.; Métay, E.; Pellet-Rostaing, S.; Lemaire, M. *J. Org. Chem.* **2009**, *74*, 3160;
b) Gracia, S.; Métay, E.; Pellet-Rostaing, S.; Lemaire, M. *Synlett* **2009**, 2617.
- ⁴³ David, E.; Lejeune, J.; Pellet-Rostaing, S.; Schulz, J.; Lemaire, M.; Chauvin, J.; Deronzier, A. *Tetrahedron Lett.* **2008**, *49*, 1860.