MOST SIGNIFICANT SCIENTIFIC ACHIEVEMENTS – Part I (2001–2019)
Jean-Cyrille HIERSO

Selection of 5 Articles

1. Hierso, J.-C.*; Fihri, A.; Ivanov, V. V.; Hanquet, B.; Pirio, N.; Amardeil, R.; Meunier, P.
"Through-space" nuclear spin–spin J_{PP} coupling in tetraphosphine ferrocenyl derivatives: A ^{31}P NMR and X-ray structure correlation study for coordination complexes.
Journal of the American Chemical Society, 2004, **126**, 11077–11087.
2. Doucet, H.; Hierso, J.-C.*
Palladium-based catalytic systems for the synthesis of conjugated enynes by Sonogashira reactions and related alkynylations.
Angewandte Chemie International Edition, 2007, **46**, 834–871.
3. Roy, D.; Mom, S.; Beaupérin, M.; Doucet, H.; Hierso, J.-C.*
A versatile palladium–triphosphane system for direct arylation of heteroarenes with chloroarenes at low catalyst loading.
Angewandte Chemie International Edition, 2010, **49**, 6650–6654.
4. Zinovyeva, V.; Vorotyntsev, M.; Bezverkhyy, I.; Chaumont, D.; Hierso, J.-C.*
Highly dispersed palladium–polypyrrole nanocomposites Pd@PPy: "in-water" synthesis and application to catalytic arylation of heteroaromatics via direct C–H bond activation.
Advanced Functional Materials, 2011, **21**, 1064–1075.
5. Roy, D.; Mom, S.; Lucas, D.; Cattey, H.; Hierso, J.-C.*; Doucet, H.
Palladium-catalyzed direct arylation of heteroaromatics with activated aryl chlorides using a sterically relieved ferrocenyl diphosphane.
ACS Catalysis, 2012, **2**, 1033–1041.

General Perspective

Since 2001, my independent research has followed an integrated approach to **transition metal chemistry, combining ligand design, homogeneous and heterogeneous catalysis**, organometallic chemistry, and functional materials. The central pillar of this research lies in the rational design of original ligands capable of finely controlling the electronic and steric environment of the metal center, with the objective of overcoming the limitations of classical catalytic systems in terms of both activity and selectivity.

The works detailed below illustrate this strategy, ranging from ferrocenyl polyphosphine chemistry to homogeneous and heterogeneous C–H functionalization, including ambiphilic hybrid ligands and the emerging chemistry of diamondoids.

1. Ferrocenyl Polyphosphines: Structuring a Field in Sustainable Catalysis
Chem. Soc. Rev. 2007; *Angew. Chem. Int. Ed.* 2010; *Org. Lett.* 2004; *Organometallics* 2003

As early as 2001, my group initiated the rational design of polydentate ferrocenyl polyphosphine ligands based on the controlled spatial proximity of donor centers. This strategy led to the development of a family of original ligands whose structural, electronic, and catalytic properties were systematically investigated.

These ligands enabled:

- Palladium-catalyzed C–C and C–N couplings at extremely low catalyst loadings (<0.01%);
- Activation of bonds traditionally considered poorly reactive, notably aromatic C–H and C–Cl bonds;
- A detailed understanding of the cooperative role of phosphorus centers in key catalytic steps.

These results contributed significantly to the development of sustainable palladium catalysis and have been widely recognized by the international community, as evidenced by authoritative reviews on Sonogashira, Heck, Suzuki, and alkynylation reactions, collectively accumulating several thousand citations.

A strong indicator of the impact and maturity of this research is the uninterrupted commercialization of these ligands by STREM Chemicals since 2011, as well as their widespread adoption by academic and industrial research groups.

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2. Low-Metal-Loading C–O, C–S, and C–N Catalysis: Mechanisms and Stability
Adv. Synth. Catal. 2011; *Chem. Eur. J.* 2011 & 2014; *Catal. Sci. Technol.* 2014

Building on these robust ferrocenyl ligands, we extended their application to C–O, C–S, and C–N coupling reactions, consistently aiming at a drastic reduction in metal loading. These studies demonstrated:

- The exceptional stabilization of palladium(0) by the ferrocene scaffold;
- The key role of local phosphorus donor density in oxidative addition and reductive elimination steps;
- The development of catalytic systems stable to air, moisture, and heat.

A major originality lies in the electrochemical and electrosynthetic analysis of these systems, conducted through interdisciplinary collaborations, which allowed access to elementary kinetic data previously unattainable for aromatic and alkyl halide substrates.

Major contribution: these works significantly advanced the mechanistic understanding of palladium catalysis while offering practical solutions for more economical and sustainable catalytic processes.

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3. Hybrid Ferrocenyl (P, N) Ligands: New Cooperative Effects in Catalysis
Organometallics 2013 & 2015; *Chem. Asian J.* 2017; *Coord. Chem. Rev.* 2017

A key structural breakthrough was the development of tetradentate hybrid ferrocenyl (P, N) ligands, diphosphine–diamine analogues designed to exploit intraligand acid/base cooperative effects. These ligands found original applications in gold catalysis, particularly in unusual C–C coupling reactions for this metal.
The originality of this approach was rapidly acknowledged, being cited as a conceptual reference in *Nature Communications* by leading groups in the field.

These studies:

- Opened new avenues toward tunable cooperative catalysis;
- Supported the ANR ALCATRAS program dedicated to robust C–H and C–O bond activation;
- Led to a landmark review article in *Coordination Chemistry Reviews*.

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4. Ambiphilic Ferrocenyl Ligands (P, B) and (N, B): Innovative Lewis Pairs
Inorg. Chem. 2017; *Chem. Commun.* 2017; *Dalton Trans.* 2019

In a deliberate thematic shift toward main-group chemistry, we developed ambiphilic ferrocenyl ligands combining donor (P or N) and acceptor (B) centers within a rigid platform.
These studies, conducted within international collaborations and protected by patent applications, enabled:

- Access to diborylated and unsymmetrical metallocenes;
- Exploration of unprecedented coordination modes;
- Investigation of electronic properties using advanced spectroscopic techniques and DFT calculations.

Conceptual breakthrough: these systems represent molecular alternatives to transition metals for small-molecule activation, with strong prospects in catalysis and chemical activation.

5. Heterogeneous C–H Functionalization: Toward Recyclable Processes
Adv. Funct. Mater. 2011; *ChemPlusChem* 2015; *Synlett* 2016

My group was among the first to translate palladium-catalyzed direct C–H functionalization into recoverable heterogeneous systems, in the absence of conventional molecular ligands.

We demonstrated:

- The efficiency of palladium@polypyrrole catalysts for direct arylation of heteroaromatics;
- The feasibility of using supported ferrocenyl polyphosphines as ligands in heterogeneous catalysis;
- The first examples of C–H arylation of heteroaromatics using chloroarenes, a particularly demanding transformation.

These works contributed to structuring the field of heterogeneous catalysis for organic synthesis and led to international recognition, notably through the publication of a special issue of *Synlett* dedicated to this topic.

Conclusion

These achievements over the period illustrate a coherent and sustained scientific contribution to ligand chemistry, transition metal catalysis, and the emergence of new catalytic paradigms, both homogeneous and heterogeneous.
They demonstrate an ability to structure research fields, to conduct well-controlled thematic shifts, and to deliver advances with significant academic, technological, and industrial impact.

MOST SIGNIFICANT SCIENTIFIC ACHIEVEMENTS – Part II (2014–2025)
Jean-Cyrille HIERSO

Selection of 5 Articles

6. Hierso, J.-C.*
Indirect Nonbonded Nuclear Spin–Spin Coupling: A Guide for the Recognition and Understanding of "Through-Space" NMR J Constants in Small Organic, Organometallic, and Coordination Compounds.
Chemical Reviews, 2014, **114**, 4838–4867.

7. Testa, C.; Gigot, E.; Genc, S.; Decréau, R.; Roger, J.; Hierso, J.-C.*
Ortho-functionalized aryltetrazines by direct palladium-catalyzed C–H halogenation: Application to fast electrophilic fluorination reactions.
Angewandte Chemie International Edition, 2016, **55**, 5555–5559.

8. Moncea, O.; Casanova-Chafer, J.; Poinsot, D.; Ochmann, L.; Mboyi, C. D.; Nasrallah, H. O.; Llobet, E.; Makni, I.; El Atrous, M.; Brandès, S.; Rousselin, Y.; Domenichini, B.; Nuns, N.; Fokin, A. A.; Schreiner, P. R.; Hierso, J.-C.*
Diamondoid Nanostructures as sp^3-Carbon-Based Gas Sensors.
Angewandte Chemie International Edition, 2019, **58**, 9933–9938.

9. Nasrallah, H. O.; Min, Y.; Lerayer, E.; Nguyen, T.-A.; Poinsot, D.; Roger, J.; Brandes, S.; Heintz, O.; Roblin, P.; Jolibois, F.; Poteau, R.; Coppel, Y.; Kahn, M. L.; Gerber, I. C.; Axet, M. R.; Serp, P.; Hierso, J.-C.*
Nanocatalysts for High Selectivity Enyne Cyclization: Oxidative Surface Reorganization of Gold Sub-2-nm Nanoparticle Networks.
JACS Au, 2021, **1**, 187–200.

10. Malkina, O. L.; Hierso, J.-C.*; Malkin, V. G.
Distinguishing "Through-Space" from "Through-Bonds" Contributions in Indirect Nuclear Spin–Spin Coupling: General Approaches Applied to Complex JPP and JPSe Scalar Couplings.
Journal of the American Chemical Society, 2022, **144**, 10768–10784.

General Perspective

These works aim to reveal, understand, and exploit the decisive role of weak interactions and ligand effects in shaping spectroscopic properties, catalytic reactivity, and the functionalities of advanced materials. They lie at the interface of fundamental chemistry, coordination chemistry, nanoscience, and sustainable applications, with a consistent guiding principle: demonstrating that noncovalent interactions—long regarded as secondary—can govern major phenomena in modern chemistry. The five selected publications illustrate this integrated approach, spanning fundamental NMR theory, nanocatalysis, chemical sensing, and biorthogonal chemistry.

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1. “Through-Space” NMR Couplings: Conceptual Clarification and New Tools
Chemical Reviews 2014; *Journal of the American Chemical Society* 2022

High-resolution nuclear magnetic resonance (NMR) spectroscopy is a cornerstone of chemistry and the life sciences. However, the physical nature of indirect nuclear spin–spin couplings has remained incompletely understood in many complex systems, particularly when covalent through-bond (TB) and nonbonded through-space (TS) pathways coexist.

The *Chemical Reviews* article (2014) provided the first comprehensive conceptual synthesis devoted to TS scalar couplings in organic, organometallic, and coordination compounds. It established:

- The generality and experimental observability of TS couplings for many nuclei (^1H, ^13C, ^19F, ^31P, ^77Se);
- Their quantitative dependence on internuclear distances;
- Their value as highly sensitive structural probes, including in hydrogen-bonded systems.

This review durably structured the field and contributed to the recognition of TS couplings as a full-fledged NMR analytical tool.
In the *JACS* article (2022), we introduced a further conceptual advance by proposing two original and complementary theoretical approaches that, for the first time, allow a quantitative decomposition of TB and TS contributions within the same real molecular system.

We demonstrated the existence of hybrid TB/TS pathways involving lone pairs of nearby heteroatoms (P, Se), revealing an unprecedented mechanism of NMR coupling transmission.

Major contribution: these studies profoundly renewed the interpretation of NMR parameters and have direct impact on ligand chemistry, coordination chemistry, and the structural analysis of complex systems.

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2. Diamondoids and sp^3 Carbon: A New Paradigm for Gas Sensors
Angew. Chem. Int. Ed. 2019 – *Hot Paper*; *Adv. Mater. Tech.* 2024; *Nanoscale* 2025

A structuring achievement concerns the introduction of functionalized diamondoids as original molecular building blocks for the design of innovative sensing materials.

We demonstrated that difunctionalized diamondoids can be:

- Assembled by vapor-phase deposition;

- Coated with palladium nanolayers, later extended to gold;
- Used to create the first chemical sensors based on sp^3 carbon.

These devices exhibit:

- Reversible NO_2 detection down to 50 ppb;
- Efficient detection of NH_3 and H_2 (25–100 ppm);
- Excellent stability under humid atmospheres;
- Ordered nanoporous architectures arising from controlled hydrogen-bonding networks.

Scientific breakthrough: this work opens a new route for chemical sensing, distinct from conventional metal oxide technologies, based on rationally designed hybrid carbon–metal architectures.

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3. Ultra-Selective Nanocatalysis: Going Beyond Homogeneous Catalysis
JACS Au 2021

In the field of sustainable catalysis, we demonstrated that controlled nanoscale structuring of catalysts enables selectivity that are inaccessible in homogeneous catalysis.

We developed an original strategy allowing:

- The synthesis of gold nanoparticles smaller than 2 nm;
- Their organization into dense networks stabilized by ditopic diamondoid ligands;
- Their use as highly selective heterogeneous precatalysts.

These nanocatalysts enable:

- Selective enyne cyclization to a five-membered conjugated diene, unattainable with homogeneous catalysts;
- A one-pot cascade reaction (cycloisomerization / Diels–Alder);
- Easy product separation and excellent recyclability.

Key contribution: this study demonstrates that ligand chemistry, transposed to the nanometer scale, enables precision heterogeneous catalysis that surpasses the limits of classical approaches.

4. “Double-Click” Tetrazines: New Architectures for Biorthogonal Chemistry
Angew. Chem. Int. Ed. 2016; *Angew. Chem. Int. Ed.* 2020 – *Hot Topic*; *Angew. Chem. Int. Ed.* 2023

A major contribution concerns the design of doubly clickable tetrazines for biorthogonal chemistry.

We developed:

- Cu-catalyzed homocoupling of *s*-aryltetrazines;
- The first identification of intramolecular π–π $[N]_8$ interactions stabilizing a rigid conformation;
- The generation, after iEDDA cycloaddition, of an original three-dimensional “staple-like” architecture.

These compounds enable:

- Programmable double-click chemistry;
- Sequential introduction of fluorophores;
- Efficient bioconjugation on antibodies.

Impact: these works opened new perspectives in biorthogonal chemistry, imaging, and the life sciences by combining weak interactions with controlled reactivity.

Conclusion

These achievements illustrate a structuring, coherent, and long-term scientific contribution, ranging from the fundamental understanding of electronic interactions to the design of catalytic systems and functional materials.
They demonstrate that mastering weak interactions—at the heart of ligand chemistry—constitutes a powerful lever for generating conceptual breakthroughs and high-impact applications in chemistry, nanoscience, and energy.