

Our Cup of Tea: Sustainable Organometallic Chemistry

What makes organometallic chemistry sustainable, or at least could make it more sustainable? A practical concept that allows us to set deliverable sustainability goals is Istvan Horváth's sustainable definition of sustainability: *Resources including energy should be used at a rate at which they are replaced naturally and the generation of waste cannot be faster than the rate of their remediation.*^[1] Significant conceptual and technological advances have been made in achieving sustainability in chemistry in academia, especially since the articulation of the field of green chemistry.^[2] In industry, it has been recognized that pushing for more sustainable chemistries and processes has a strong business case - not only does it lower the cost of goods and environmental footprints, it also results in a stronger brand, enhanced customer loyalty, and improves an organization's position in the talent market.^[3]

Organometallic chemistry has played an important role in green chemistry, particularly in the area of metal catalysis and energy chemistry.^[4] However, the bar for success is only getting higher to deliver innovations that fulfill Horváth's definition of sustainability. Trying to improve an unsustainable reaction ultimately does not make it more sustainable. To achieve truly sustainable organometallic chemistry, a holistic approach is needed, which requires the invention of new solvents, ligands, metal catalysts, substrates, and energy sources that are renewable and do not generate waste, whether it is deemed toxic or not (Figure 1).

This *Organometallics* Special Issue, "Sustainable Organometallic Chemistry," features 18 contributions focusing on organometallic systems and reactions in which one or several components are sustainable. This includes in particular a switch to earth-abundant metals, but also green ligands, biobased solvents and nonfossil substrates. The contributed articles are from all over the world, highlighting that sustainability is a *global issue*, which is being actively studied by groups everywhere. We hope you will enjoy this lovely mixture of articles, perhaps together with a nice cup of tea!

Sustainable metal catalysis

Catalysis with metals that are not scarce, depleting, or toxic is crucial in delivering sustainable organometallic chemistry. First-row 3d transition metals have relatively high abundance, low toxicity, and show less harmful effects on the environment than their 4d and 5d counterparts.^[5] First up from the first row is manganese in the report from **Pidko**

and coworkers from Delft University of Technology and Wageningen University, who studied the mechanism of ketone reduction by a homogeneous Mn catalyst (DOI: [10.1021/acs.organomet.2c00077](https://doi.org/10.1021/acs.organomet.2c00077)). Their analysis points to the possibility of a Meerwein-Ponndorf-Verley (MPV) type mechanism, where the ketone substrate is reduced by a Mn-alkoxide adduct via a solvent-assisted hydride shift, in contrast to the mechanisms conventionally proposed for Mn-based metal-ligand cooperative transfer hydrogenation catalysts. The authors find that the solvent significantly lowers the transition-state barrier by stabilizing anionic intermediates via hydrogen bonding interactions. This study illustrates that advanced computational methods that accurately take solvent effects into account can support the feasibility of a previously discarded mechanism. *Or to say it otherwise, the solvent solved it!*

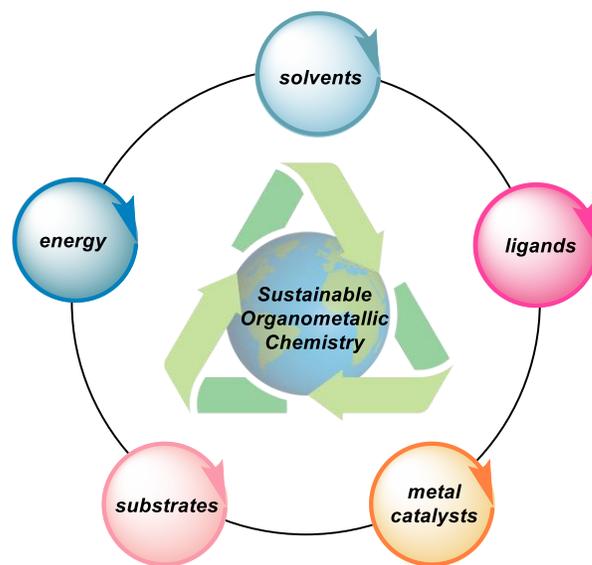


Figure 1. Sustainable organometallic chemistry involves different flavors of innovation: the design of solvents, ligands, metal catalysts, substrates, and energy sources that are renewable.

The activity of a catalyst is highly dependent on the ligand, and in some cases, the ligand gets actively involved in a reaction, leading to a bifunctional system. **Bera and coworkers from the Indian Institute of Technology Kanpur** report a Mn complex with a naphthyridine-*N*-oxide proton responsive unit as a bifunctional catalyst for the α -

alkylation of ketones, including bioactive steroids pregnenolone and progesterone (DOI: [10.1021/acs.organomet.2c00085](https://doi.org/10.1021/acs.organomet.2c00085)). NMR and UV-Vis measurements support the solution-phase equilibrium between the protonated (lactam) and the deprotonated (lactim) forms. The catalyst without the proton-responsive hydroxy unit is shown to be significantly less active, highlighting the crucial role of the OH group in the catalytic mechanism. *There is no doubt, bifunctional is beautiful!*

The versatile chemistry of manganese is also shown in the contribution by **Rueping and colleagues from King Abdullah University of Science and Technology and RWTH Aachen University**, who report the intramolecular N-heterocyclization of amino alcohols to the corresponding amides and alcohols, using a well-defined Mn complex (DOI: [10.1021/acs.organomet.2c00027](https://doi.org/10.1021/acs.organomet.2c00027)). The reaction occurs with low catalyst loadings and catalytic base, and divergent reactivity is achieved with judicious catalyst and solvent choice. *Consider magnificent manganese for your next synthetic project!*

Moving one step further along the first row of transition metals, we get to iron, the most abundant transition metal in the universe!^[6] **Neely and coworkers at Saint Louis University and University of Missouri-St. Louis** report the isolation of a mononuclear iron azametallacyclobutane complex, with reactivity that diverges from its early transition metal group 4 counterparts (DOI: [10.1021/acs.organomet.2c00151](https://doi.org/10.1021/acs.organomet.2c00151)). When treated with unsaturated organic substrates, the iron azametallacyclobutene complex undergoes insertion into the metal-nitrogen bond, whereas its zirconium and titanium analogs undergo migratory insertion into the metal-carbon bond. These observations shed light on the mechanisms of iron-mediated C-N bond formation. *Who knows, maybe iron could soon become the most abundant metal in your lab?*

Cobalt is not as ubiquitous as iron, but its properties make it useful as an alternative for reactions that rely on rhodium, such as hydrogenations. **Hopmann from UiT -The Arctic University of Norway, Chirik from Princeton University, and their coworkers** report experimental and computational insights into the cobalt-catalyzed hydrogenation of enamides (DOI: [10.1021/acs.organomet.2c00180](https://doi.org/10.1021/acs.organomet.2c00180)). The authors show that both redox- and nonredox hydrogenation pathways are accessible, highlighting that earth-abundant metals such as cobalt may exhibit more complex mechanistic routes than the classic two-electron redox pathways known from many precious metals. *Clearly, redox reactions require more than a reductionist approach!*

Cobalt can also catalyze other challenging reactions, such as carbon-carbon bond formations, however, in these cases sterically demanding substrates often provide poor yields – until now. **Fout and her team from the University of Illinois, Urbana-Champaign**, report a cobalt-catalyzed catalytic Kumada coupling of aryl Grignard reagents to sterically

encumbered alkyl halides (DOI: [10.1021/acs.organomet.1c00513](https://doi.org/10.1021/acs.organomet.1c00513)). The developed method is quite valuable synthetically, allowing for installation of neopentyl and other challenging groups on bulky organic substrates, resulting in formation of quaternary centers. *Certainly, cobalt is not afraid of hard work!*

Cobalt can also tackle formation of carbon-boron bonds, including formation of polyboron intermediates with multiple C-B units, which are useful precursors for stepwise functionalizing. **Ge and his team from the National University of Singapore** (DOI: [10.1021/acs.organomet.2c00053](https://doi.org/10.1021/acs.organomet.2c00053)) report a new and selective cobalt-catalyzed 1,1,3-triborylation of terminal alkynes to form 1,1,3-triborylalkanes. The authors also show that the polyboron intermediates can undergo sequential C-C and C-heteroatom bond-forming reactions, enabling selective functionalization. *Cobalt and boron are definitely not a boring couple!*

Can nickel replace palladium for C-C coupling reactions? The answer to that question is investigated by **Diao and coworkers at New York University** via reductive elimination from d⁸ organonickel complexes (DOI: [10.1021/acs.organomet.2c00091](https://doi.org/10.1021/acs.organomet.2c00091)). By using square-planar biOx and (box)Ni(II)-dialkyl complexes and alkyl iodide as the oxidant, the mechanism of this elementary step is unveiled. The insights from this study have the potential to inform future catalyst design for important nickel-mediated C-C bond formations. *Wouldn't you want a nickel for every C-C coupling in the world?*

Just as mechanistic studies can guide catalyst design, machine learning can be an equally invaluable tool to predict reaction outcomes. In the contribution by **Stevens and his team at Bristol Myers Squibb**, an expansive dataset in a nickel-catalyzed borylation is used to train machine learning models to identify important parameters in the phosphine ligand used in the reaction that can reliably predict outcomes to optimize performance (DOI: [10.1021/acs.organomet.2c00089](https://doi.org/10.1021/acs.organomet.2c00089)). These machine learning models are also successful in predicting reaction yields using ligands that are not included in the model training. *What's cooler than predicting something can be cool before it is even cool?*

Last but not least in the first row of transition metals is copper. **Lázaro, Caballero, Pérez, Lledós, and coworkers** from Universidad de Huelva, Compañía Española de Petróleos S.A., and Universitat Autònoma de Barcelona report the direct oxidation of benzene to phenol mediated by TpBr₃Cu(NCMe) in the presence of ascorbic acid (DOI: [10.1021/acs.organomet.2c00202](https://doi.org/10.1021/acs.organomet.2c00202)). Based on computational results, a dinuclear species is proposed to be the active catalyst, which promotes C-H activation and phenol formation. The results show that a synthetic complex can promote the same reaction as binuclear copper mono-oxygenases. *What a perfect match: sustainability & biomimetics!*

Molybdenum is a second-row transition metal, but can nonetheless serve as a promising substitute for precious metals, owing to its low toxicity and cost—it is even cheaper than cobalt! **Beller, Junge, and their team at the Leibniz Institute for Catalysis** report Mo PNP pincer complexes as catalysts for the semi-hydrogenation of diaryl alkynes (DOI: [10.1021/acs.organomet.1c00709](https://doi.org/10.1021/acs.organomet.1c00709)). The efficiencies of the different Mo compounds depend on the steric bulk on the ligand, but catalytic reactions proceed with good chemoselectivity against overreduction and high (*Z*)-selectivity. In addition, end of reaction (*Z*) to (*E*) isomerization is not observed, in contrast to some 1st row metal systems. *Being second row does not mean you cannot be first choice!*

How about non-transition metals? Bismuth is an interesting example, which, although placed right next to highly toxic lead, is considered a “green metal” due to its low toxicity—think about its use in Pepto Bismol.^[7] Bismuth compounds are easy to handle, have relatively low cost, and interesting properties.^[7] **Cornella and his coworkers from Max-Planck-Institut für Kohlenforschung** report a series of cationic fluorotriarylbi-muthonium salts bearing differently substituted aryl groups, with a detailed analysis of the structural aspects and the behavior in solution (DOI: [10.1021/acs.organomet.2c00135](https://doi.org/10.1021/acs.organomet.2c00135)). Through fine-tuning of the substituents, the authors are able to isolate a unique mononuclear nonstabilized fluorotriarylbi-muthonium cation, which is remarkably stable at room temperature both in solution and in the solid state. This insights are relevant for designing catalytic C–F bond formation reactions based on bismuth. *Maybe bismuth can sooth your sustainability distress?*

Sustainable ligands, substrates, and solvents

To synthesize sustainable compounds, renewable starting materials are needed. In particular, it is important to find carbon-based starting materials that do not originate from fossil resources. A renewable carbon source that is increasingly used in chemical synthesis is carbon dioxide, which is so abundant that it is essentially impossible to deplete. In the contribution by **Popp and coworkers from West Virginia University**, copper-catalyzed fixation of CO₂ leads to formation of synthetically useful α -quaternary carboxylic acids (DOI: [10.1021/acs.organomet.2c00184](https://doi.org/10.1021/acs.organomet.2c00184)). Interestingly, the authors show that low CO₂ concentrations are critical to achieve efficient boracarboxylation of sterically demanding substrates. *Sometimes less is more!*

Photocatalytic CO₂ reduction with iron is achieved in the report by **Saito, Jung, and their colleagues at Nagoya University and Toyota Central R&D Labs** (DOI: [10.1021/acs.organomet.2c00171](https://doi.org/10.1021/acs.organomet.2c00171)). The combination of an iron complex containing a tetradentate PNNP ligand and a photosensitizer is shown to catalyze the photochemical CO₂ reduction to produce mainly carbon monoxide. The bulky phosphine ligands in the iron complex significantly improve

catalyst stability. The direct electron transfer from the reduced photocatalyst to the Fe catalyst is observed using picotAS measurements. *What a sustainability combo: iron, light, and CO₂!*

An important parameter to be considered in the development of sustainable reactions is the energy required to make starting materials. For example, hydrosilanes are useful reductants in organic synthesis, but currently they are produced via energy-demanding processes. A big step forward is the report by **Cantat and coworkers from Université Paris-Saclay**, who have developed an iridium-catalyzed process for hydrogenolysis of silyl triflates into hydrosilanes under mild conditions, involving room temperature and one bar H₂ (DOI: [10.1021/acs.organomet.1c00576](https://doi.org/10.1021/acs.organomet.1c00576)). DFT calculations show that the active species is a neutral iridium(III) dihydride complex, with the developed reaction being faster than for other reported catalysts. *Less energy, but more speed, sounds like a sustainability dream!*

Amines are common functionalities in organic compounds, but their traditional synthesis has drawbacks, calling for the development of more efficient methods. A catalytic, atom-economical approach is hydroaminoalkylation, involving functionalization of unprotected amines with alkenes, which also avoids additives such as bases and oxidants. **Schafer and her team at University of British Columbia** have investigated the use of little explored *N,N*-chelated tantalum complexes in the hydroaminoalkylation reaction (DOI: [10.1021/acs.organomet.2c00043](https://doi.org/10.1021/acs.organomet.2c00043)). The results provide insights into the effect of steric bulk on the reactivity and show a broad substrate scope with excellent regioselectivity. *Tantalizing tantalum makes amiable amines!*

An optimally sustainable reaction requires that the catalyst ligands also come from renewable resources. A notable contribution in this direction is the development of *N*-heterocyclic ligands based on a xanthine scaffold reported by **Szostak and coworkers from Rutgers University and their collaborators from Opole University, University of Wrocław, and Wrocław University of Science and Technology** (DOI: [10.1021/acs.organomet.2c00019](https://doi.org/10.1021/acs.organomet.2c00019)). The natural products caffeine and theophylline are employed to develop air- and moisture-stable, half-sandwich cyclopentadienyl nickel–*N*-heterocyclic carbene complexes, which show high activity in Suzuki–Miyaura cross-coupling. *Maybe all your next ligand synthesis needs is a drop of coffee or spot of tea?*

This brings us to the solvent used in chemical reactions, which of course should be green and sustainable too. As much as 80 to 90% of mass utilization in a typical pharmaceutical or fine chemical operation is the solvent, which also accounts for water used in extractions and other steps.^[8] Thus, efforts to find alternative and sustainable solvents are of high interest. In the contribution by **Gevorgyan and coworkers from UiT-The Arctic University**, it is demonstrated that the Buchwald–Hartwig amination can be run in

vegetable oils and related lipids, which in many cases outperform traditional fossil-based solvents (DOI: [10.1021/acs.organomet.1c00517](https://doi.org/10.1021/acs.organomet.1c00517)). Interestingly, the authors identified a “magic mix” of amphiphilic trace ingredients that can improve the yields of the Buchwald-Hartwig amination, whether performed in traditional or green solvents. *Indeed, sustainable chemistry can be magical!*

The 18 contributions in this Special Issue highlight the current progress in using abundant and more sustainable components in organometallic chemistry. We are looking forward to seeing how this field develops and we are optimistic that the concepts, strategies, and challenges revealed in these reports will serve as opportunities for further development as we together aim to truly achieve sustainable sustainability. *Certainly our cup of tea!*

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Notes

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^[1] Cséfalvay, E.; Akien, G. R.; Qi, L.; Horváth, I. T. Definition and application of ethanol equivalent: Sustainability performance metrics for biomass conversion to carbon-based fuels and chemicals. *Catalysis Today* **2015**, *239*, 50-55.

^[2] (a) Anastas, P.; Eghbali, N. *Chem. Soc. Rev.* **2010**, *39*, 301-312. (b) Anastas, P. T.; Zimmerman, J. B. The Periodic Table of the Elements of Green and Sustainable Chemistry. *Green Chem.* **2019**, *21*, 6545.

^[3] Winston, A. S. The Big Pivot: Radically Practical Strategies for a Hotter, Scarcer, and More Open World; Harvard Business Review Press, **2014**.

^[4] (a) Crabtree, R. H. An Organometallic Future in Green and Energy Chemistry? *Organometallics*, **2011**, *30*, 17-19. (b) Parshall, G. W.;

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REFERENCES

Putscher, R. E. Organometallic Chemistry and Catalysis in Industry. *Organometallics*, **1986**, *3*, 189-191.

^[5] Alig, L.; Fritz, M.; Schneider, S. First-Row Transition Metal (De)Hydrogenation Catalysis Based On Functional Pincer Ligands, *Chem. Rev.* **2019**, *119*, 4, 2681–2751.

^[6] Anders, E.; Grevesse, N.; Abundances of the elements: Meteoritic and solar, *Geochimica et Cosmochimica Acta* **1989**, *53*, 197-214,

^[7] Mohan, R. Green Bismuth, *Nature Chemistry* **2010**, *2*, 336.

^[8] Constable, D. J. C.; Jimenez-Gonzalez; Henderson, R. K. Perspective on Solvent Use in the Pharmaceutical Industry, *Org. Process Res. Dev.* **2007**, *11*, 1, 133–137.