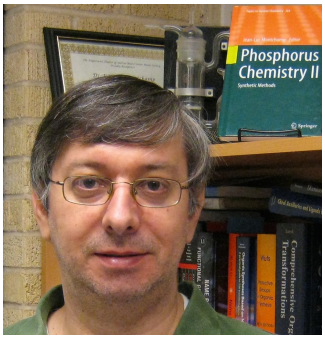

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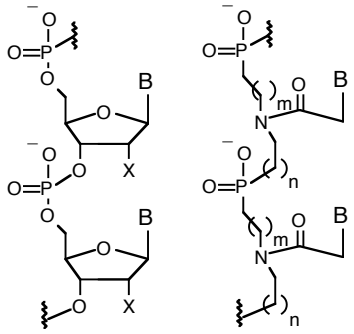
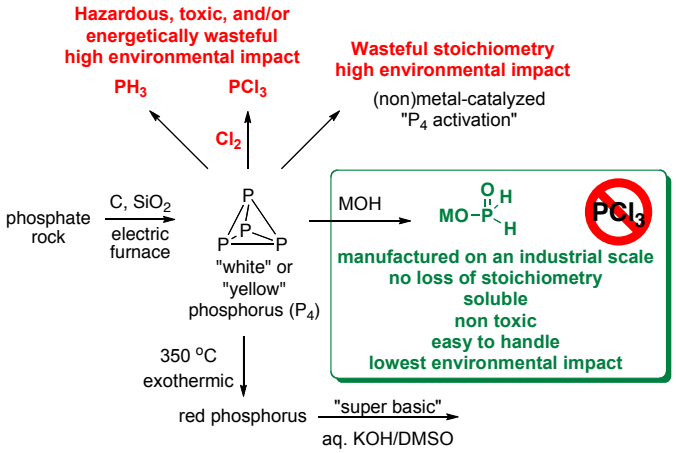


Phosphorus

Our group's research interests are in the areas of organophosphorus chemistry, and bio-organic/medicinal chemistry. The core of our program in chemical biology focuses on the mechanism-based design, synthesis and evaluation of biologically active molecules such as enzyme inhibitors, receptors agonists and antagonists, and the development of novel antisense oligonucleotides with emphasis on the application of automated synthesis and combinatorial techniques whenever possible.

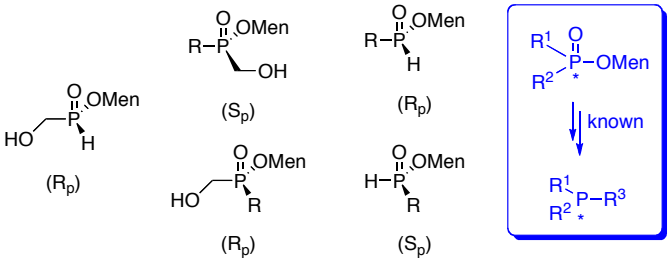
Medicinal Chemistry. Unnatural compounds are synthesized to probe or modulate various biological processes. Applications of this research range from the elucidation of enzyme mechanisms to the preparation of molecules with potential medicinal use (anticancer, antiparasite, immunosuppressant, antisense, GABA analogs, bisphosphonates). One such medicinally oriented goal is the preparation and evaluation of new hydrolytically stable antisense oligonucleotides for sequence specific complexation to RNA and DNA targets. Another area is the study of *H*-phosphinates as precursors of biologically active phosphonates and bis-phosphonates.

Organophosphorus Chemistry. Our overarching research theme concerns general organophosphorus chemistry and associated synthetic methodology development, which is driven by two main objectives: firstly, the synthesis of *P*-asymmetric compounds to be ultimately used in catalytic asymmetric transformations, including transition metal-catalyzed reactions, and secondly, the building of a methodology based on phosphorus compounds for organic synthesis as well as for the preparation of compounds possessing potential biological activity. Industrially, organophosphorus compounds used in pesticides, flame-retardants, extractants, etc. are all currently manufactured through phosphorus trichloride. Our group has developed an alternative strategy based on phosphinates (hypophosphites) as starting materials, combined with a portfolio of novel reactions.

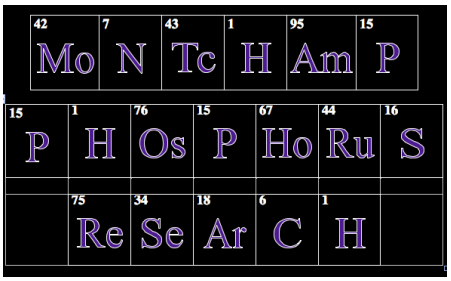


Our program toward the development of new methodology for the synthesis of *H*-phosphinic acids has led to several novel reactions, including the palladium-catalyzed cross-coupling of hypophosphorous derivatives with aryl, benzylic, and alkenyl electrophiles, and the room temperature radical addition of hypophosphites to olefins, to name a few. More recently we have uncovered new catalytic phosphorus-carbon bond-forming reactions via the hydrophosphinylation of unsaturated compounds, using palladium, nickel, and manganese catalysts. All our reactions are also applied to the synthesis of biologically active compounds. Asymmetric

versions of these new reactions are also being developed for the preparation of *P*-asymmetric building blocks.



Combining the above research directions into one research program provides valuable advantages. Because phosphorus is ubiquitous in nature, a variety of molecules can be designed to achieve some specific biological effect. To achieve the efficient synthesis of such compounds, new synthetic routes will be required, which could borrow from our own synthetic methodologies. Because of our interests in the preparation of phosphorus-containing biologically-active compounds, target-driven methodology development is also conducted in our laboratory. In general, a combination of organic synthesis, methodology, and chemical biology, will be used to pursue our objectives.



Selected Publications

"Manganese-Catalyzed and Mediated Synthesis of Arylphosphinates and Related Compounds", Berger, O.; Montchamp, J.-L. *J. Org. Chem.* **2019**, *84*, 9239-9256.

"On the Cost of Academic Methodologies", Berger, O.; Winters, K. R.; Sabourin, A,; Montchamp, J.-L. *Org. Chem. Front.* **2019**, *6*, 2095-2108.

"Challenges and solutions in phosphinate chemistry", Montchamp, J.-L. *Pure Appl. Chem.* **2019**, *91*, 113-120.

"Manganese-Mediated Homolytic Aromatic Substitution With Phosphinylidenes", Berger, O.; Montchamp, J.-L. *Chem. Rec.* **2017**, *17*, 1203-1212.

"Palladium-Catalyzed Allylation/Benzylation of *H*-Phosphinate Esters with Alcohols", Fers-Lidou, A.; Berger, O.; Montchamp, J.-L. *Molecules* **2016**, *21*, 1295-1309.

"General Synthesis of *P*-Stereogenic Compounds: The Menthyl Phosphinate Approach", Berger, O.; Montchamp, J.-L. *Org. Biomol. Chem.* **2016**, *14*, 7552-7562.

"P(=O)H to P-OH Tautomerism: A Theoretical and Experimental Study", Janesko, B. J.; Fisher, H. C.; Bridle, M. J.; Montchamp, J.-L. *J. Org. Chem.* **2015**, *80*, 10025-10032.

"Development of a New Family of Chiral Auxiliary", Gelat, F.; Richard, V.; Berger, O.; Montchamp, J.-L. *Org. Lett.* **2015**, *17*, 1819-1821.

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"A General Strategy for the Synthesis of *P*-Stereogenic Compounds", Berger, O.; Montchamp, J.-L. *Angew. Chem. Int. Ed.* **2013**, *52*, 11377-11380.

"Hydrophosphinylation of Unactivated Terminal Alkenes Catalyzed by Nickel Chloride", Ortial, S.; Fisher, H. C.; Montchamp, J.-L. *J. Org. Chem.* **2013**, *78*, 6599-6608.

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