

Iron-Catalyzed Intermolecular [2+2] Cycloadditions of Unactivated Alkenes

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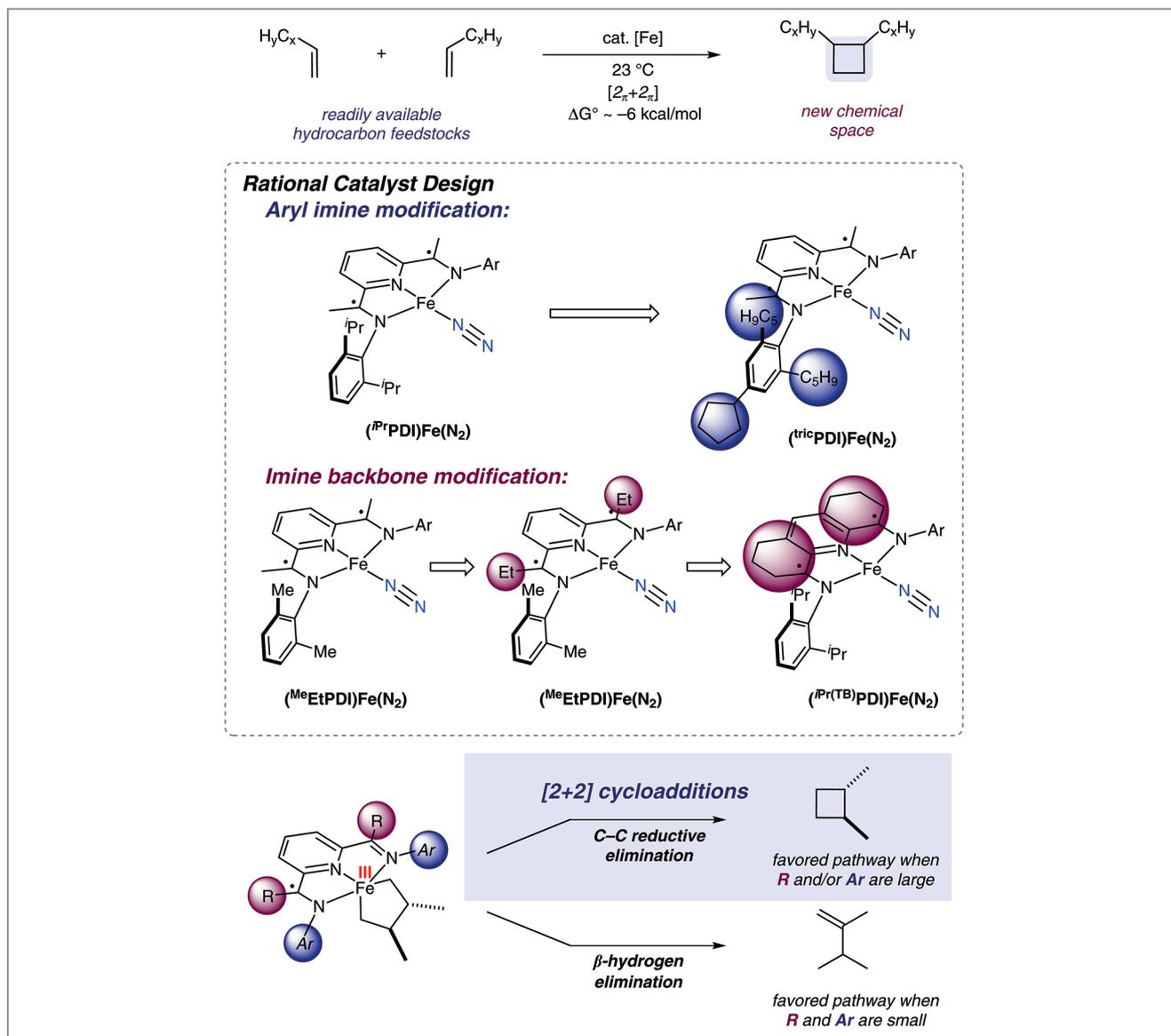
The thermal [2+2] cycloaddition of alkenes leading to cyclobutanes remains a big challenge for chemists as current methodologies rely on photochemical activation and substrates bearing chromophores. For this reason, unactivated alkenes, which are available in large quantities from natural resources, have been outside the scope of [2+2] cycloaddition reactions so far. Recently, a new breakthrough methodology for performing this transformation has been described in a *Science* paper published by Professor Paul Chirik and members of his group from Princeton University (USA). This Fe-catalyzed work is an example of chemistry that has been of long-standing interest to the Chirik group: to develop sustainable catalytic methods employing earth-abundant and environmentally benign first-row transition metals that not only have the potential to replace existing technologies requiring precious metals, but to lead to the discovery of new processes previously unobserved with any catalyst. Professor Chirik said: “Unfunctionalized alkenes and dienes are an attractive substrate class as they are derived from petrochemical and natural sources and are produced on the metric tonne scale annually.” Professor Chirik explained that the development of vast global shale gas reserves and intense efforts for the conversion of methane into higher hydrocarbons has revolutionized supply and created a glut of these feedstocks that will likely only increase in the foreseeable future. Professor Chirik continued: “The realization of new chemical transformations that convert these simple feedstocks into more value-added products is required in order to curb on-site flaring, a practice that currently consumes approximately \$30 billion USD annually and is a major source of CO₂ emissions.”

The synthesis and reactivity of reduced pyridine(diimine) iron dinitrogen compounds in the Chirik group has served as the inspiration for many developments.

Dr. Marco Bouwkamp was the lead investigator who first discovered the unique reactivity of ^{iPr}PDIFeN₂ to form cyclobutanes from tethered α-olefins (*J. Am. Chem. Soc.* **2006**, *128*, 13340). “Since that initial breakthrough,” said Professor Chirik, “a team of graduate students and postdoctoral researchers have tackled the challenge of understanding the distinctive properties of this [2+2] cycloaddition including a mechanistic overview of the process by Dr. Jordan M. Hoyt (*J. Am. Chem.*

Soc. **2013**, *135*, 4862) and extension of this reactivity to the analogous cobalt pyridine(diimine) platform by Dr. Valerie A. Schmidt (*J. Am. Chem. Soc.* **2015**, *137*, 7903).” During the course of this cobalt study, a new pyridine(diimine) ligand was synthesized in which the 2,6-diisopropyl groups of the aryl imine were replaced with cyclopentyl groups. Professor Chirik said: “While a seemingly subtle change, this cyclopentyl-substituted cobalt compound proved to have an activity comparable to that of ^{iPr}PDIFeN₂, which was previously identified as the most active [2+2] catalyst.” Another significant advance in this project was made by Dr. Sarah K. Russell with the synthesis of ^{Me}PDIFeN₂ (*Inorg. Chem.* **2010**, *49*, 2782) and the discovery that it was an effective catalyst for the [2+2] cycloaddition of 1,3-butadiene and ethylene to give vinyl cyclobutane (*J. Am. Chem. Soc.* **2011**, *133*, 8858). “Extending the reactivity beyond this singular intermolecular reaction proved challenging, as a loss in selectivity and activity was observed upon changing of the substrates,” explained Professor Chirik.

In order to overcome these limitations and with mechanistic insights in hand, new catalysts were rationally designed by the group and the reaction conditions were improved (Scheme 1). Professor Chirik said: “Inspired by the results with cobalt, an iron pre-catalyst bearing the 2,4,6-tricyclopentyl groups on the aryl imine moiety (^{tricyclopentyl}PDIFeN₂) was prepared and found to be active and very selective for the intermolecular [2+2] cycloaddition of alkenes.” Solvent-free conditions were used in order to maximize the activity and remove any waste generation from the reaction. A second catalyst was developed for this transformation and was found to have higher activity, but lower selectivity for the cyclobutane products. Professor Chirik explained: “This was achieved by modifying the ^{Me}PDIFeN₂ catalysts with larger imine ethyl groups forming ^{MeEt}PDIFeN₂. This substitution prevents imine dissociation from the metal center and minimizes byproduct formation.” In order to further prevent imine dissociation, an iron pre-catalyst was prepared in which the imine group was ‘tied-back’ and attached to the pyridine ring (^{iPr(TB)}PDIFeN₂). This modification enabled a significant improvement in the scope and selectivity of diene–alkene [2+2] cycloadditions. Professor Chirik concluded: “With these developed catalysts in hand, we evaluated a series of naturally and petrochemically derived commodity chemicals for the formation of cyclobutanes.



Scheme 1

Future catalyst development has the potential to further expand the scope of alkene and diene substrates in thermal [2+2] cycloaddition reactions.”

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About the authors



Prof. P. J. Chirik

Peter J. W. Debye Professor. In 2011, he relocated to Princeton University (USA) and is currently the Edwards S. Sanford Professor of Chemistry, Associate Director of the Andlinger Center for Energy and Environment and Editor-in-Chief of *Organometallics*.

Valerie A. Schmidt graduated from Towson University (USA) in 2007 before moving to North Carolina to pursue a Ph.D. under the tutelage of Professor Erik J. Alexanian at the University of North Carolina at Chapel Hill (USA). Valerie joined the Chirik group for her postdoctoral studies in 2013 and is a recipient of an NIH NRSA Postdoctoral Fellowship.



Dr. V. A. Schmidt



Dr. J. M. Hoyt

Jordan M. Hoyt attended Florida State University (USA) as an undergraduate where he worked in the lab of Michael Shatruk. After graduating in 2010, Jordan joined the lab of Paul J. Chirik at Cornell University (USA) and shortly thereafter moved with the Chirik group to Princeton University (USA) where he received his Ph.D. in spring 2015.

Aaron M. Tondreau graduated from California State University, Bakersfield (USA) before joining the Chirik group in 2006 where he developed base-metal-catalyzed hydrosilylation reactions. Aaron then went on to pursue postdoctoral studies with Professor Hansjörg Grützmacher at ETH Zurich (Switzerland) and is currently employed at Los Alamos National Laboratory (USA) working with Dr. James Boncella.