**2014 ACS GCI Pharmaceutical Roundtable Research Grant for Iron Catalysis**

The ACS GCI Pharmaceutical Roundtable is seeking to fund a 1-2 year R&D program to address the Roundtable's initiatives in iron catalysis. Proposals should target the development of innovative and novel iron-catalyzed coupling reactions or catalytic iron based alternatives for current coupling technologies that enjoy widespread use. Proposals are invited from public and private institutions of higher education worldwide. This collaborative project is intended for a student within the selected Principal Investigator's research group. One grant in the amount of $100,000 will be awarded to support execution of research for a period of 1-2 years. Deadline for receipt of proposals is August 22, 2014 at 5 PM EDT (GMT-4). Proposals not received by the deadline will not be considered. Submissions must be a single pdf file submitted via email to gcipr@acs.org. The Principal Investigator with the selected proposal will be notified in November 2014 of the decision**.** It is expected that research will commence in the principal investigator's lab by February 2015 and last approximately 1-2 years.

**Requirements for Submission:**

Proposals will only be accepted from public and private institutions of higher education. The grant is not limited to institutions in the United States. Proposals must be submitted by email to gcipr@acs.org through the appropriate institutional office for external funding. For international submissions with no comparable office, submit a pdf of a letter signed by an appropriate university official recognizing the terms of the grant.

**Detailed Project Description:**

Metal catalyzed coupling reactions are an indispensable tool for the synthetic organic chemist. The numerous modes of chemical activation offered by metal catalysts offer a vast range of synthetic transformations. In many instances by tuning the oxidation state, counterion, and the steric and electronic properties of ligands, a single metal can catalyze reactions across numerous activation modes. With such widespread use in the pharmaceutical industry, development of more environmentally benign metal catalyzed coupling processes would have a significant impact on advancement of Green Chemistry principles.

A serious concern facing the pharmaceutical manufacturing community in 2014 (and the foreseeable future) is a lack of widespread, proven, and robust methods for catalytic iron based coupling protocols. Despite the demonstrated utility of transition metals for a wide range of useful transformations, the drivers for replacement of precious metals (such as Pd, Ru, Rh, Ir, etc.) with Fe alternatives are numerous. High cost, fluctuating global supply, human toxicity, and limited natural abundance are just a few of the drawbacks associated with precious metals. In response, we wish to address the entire space of chemical activation with iron catalysis toward *catalytic coupling processes*.

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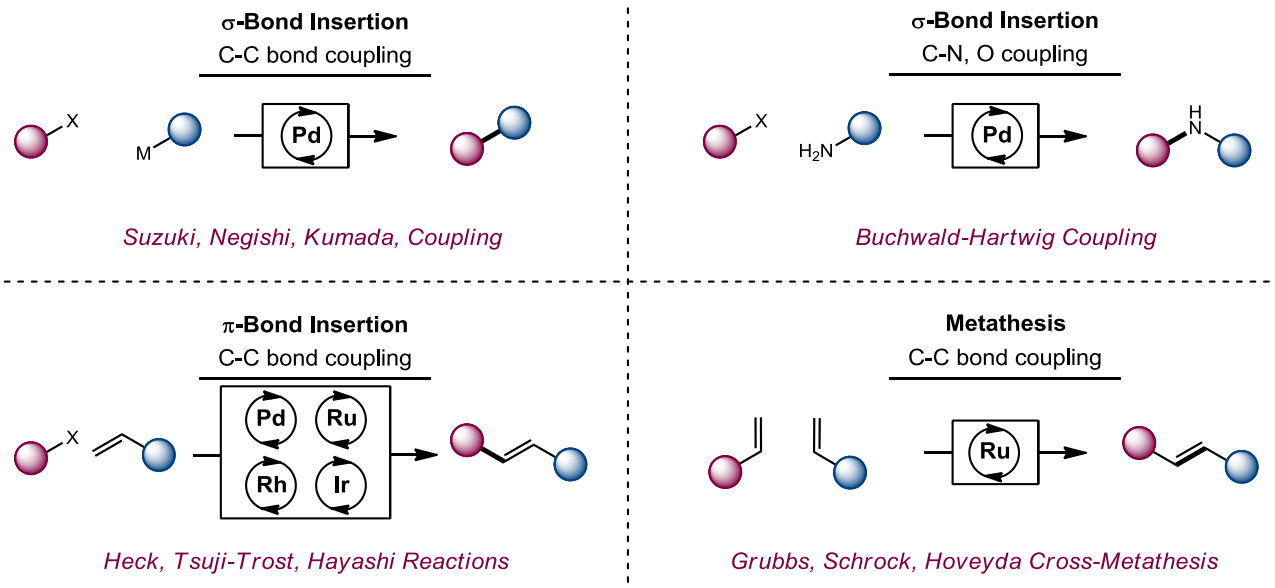
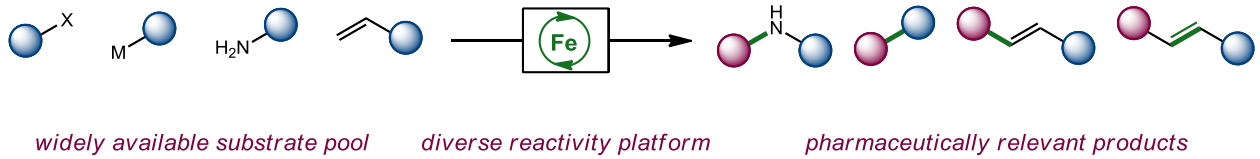
**Scheme 1. Reaction manifolds for metal-catalyzed coupling reactions in the pharmaceutical industry**




In sharp contrast to the typical protocols currently being utilized by the pharmaceutical industry, a more desirable future state involves:

- Access to current reaction manifolds and substrate pools with more environmentally benign iron catalysts.
- New coupling technologies that employ iron catalysts;
- Expanded substrate compatibility to include heterocyclic motifs commonly found in drug substances;
- Simple and inexpensive nitrogen and/or oxygen based ligands;
- Lower oxygen sensitivity;
- Near ambient temperature reactions;
- Environmentally responsible solvent systems.

**Scheme 2. Desired future state for metal catalyzed coupling reactions.**




The overarching theme of this proposal is to support extension of iron catalysis into the pharma space by developing conditions for iron based coupling reactions applied to high value, pharmaceutically-relevant substrates, such as heterocyclic aromatic compounds. Additional favorable criteria are outlined below:

- Widespread utility/ease of access: Ligands and metal sources should be readily available from commercial sources or prepared with a minimal number of steps from inexpensive starting materials;
- Substrate scope: The scope should be significantly diverse to accommodate a wide range of functional groups and heterocycles with a preference for pharmaceutically relevant scaffolds;

- The proposed methods/innovations should employ greener solvents to the extent possible. For further solvent guidance, refer to the ACS GCI Pharmaceutical Roundtable Solvent Selection Guide.
- Simplification of work-up/purification methods.

**Project Goal:**
Provide alternative conditions to commonly employed metal catalyzed coupling reactions or new coupling technologies that employ iron catalysts. The solutions should be applicable to a wide variety of substrates and ideally, should employ readily-available N- and/or O-based ligands.

**Project Timeline:**
It is expected that 1-2 years of research support will be sufficient to provide progress toward intended goals.

**Proposal Format:**
A maximum of 6 pages, as described below, plus CVs is requested. All of the information below must be submitted as a single PDF file. All components described in sections A, B, and C must be included in the same PDF file to assure the proposal is reviewed in its entirety.

A) Title Page (1 page, 12 pt font, 1-inch margins)
1. Project Title:
2. Principal Investigator
3. Title / Position(s)
4. Telephone Number(s)
5. Fax Number(s)
6. Postal Mailing Address
7. E-Mail Address
8. Research Group website

B) Proposed Plan of Work *(5 pages, 12 pt font, 1-inch margins)*
1. Abstract: Summary statement of how the proposed work meets the overall criteria of identification and development of NPMC alternatives for widely employed Transition Metal (TM) catalyzed cross-coupling reactions. (500 words or less)
2. Background: Provide a brief assessment of the proposed project in the context of the current state of knowledge, demonstrating awareness of green chemistry improvements over current technology. (limit to 1 page or less)
3. Objectives: Briefly state the project objectives.
4. Project Approach: Include specific aims, investigations planned, and preliminary results.
5. References
6. Project Timeline
7. Estimated Budget: The total amount requested would include all direct and indirect costs, including fringe benefits, student assistantships, etc. The total award is limited to $100,000 for a grant period of 12 to 24 months.
    a. Institutional overhead costs (indirect costs) are limited to 10% of the grant amount.

b. Funding would start in February 2015, or later as agreed between the Principal Investigator and the Roundtable.
c. Post-doctoral associate salary and benefits are supported.
d. Graduate student stipend and benefits are supported. Proposals for support of advanced graduate students are highly favored.
e. PI salary supplements will not be supported.
f. Laboratory supplies and instrument use charges are supported.
g. No funds may be allocated for travel, equipment purchase or repair, or administrative support.

8. Current funding list for the PI including title of grant award, agency, award amount and duration – limit to 1 page or less
9. Brief facilities description for the PI – limit to one page or less
10. Listing of any existing background intellectual property and/or collaborations that might limit the freedom to operate any of the results arising from any research funded by ACS GCI.

C) Curriculum Vitae of Project Team Members: Please submit a two page curriculum vitae of all project team members. (Does not count toward your page limit.)

**Report Requirements:**

- As a collaborative research project, the Roundtable will work closely with the principal investigator and student(s) to provide industrial direction, when appropriate, in a manner that respects the independence of the researcher/student.
    - Teleconferences with Roundtable members will be held monthly to discuss project status, provide suggestions and feedback pertaining to reaction conditions/optimization, solvent selection and pharmaceutically relevant substrates.
    - Written progress updates are due monthly from initiation of research for discussion during teleconferences.
    - Updates are to include research milestones/significant outcomes, summary of progress to date noting any deviations from the proposal, and research plans for upcoming months.
- A final comprehensive report including research outcomes and final budget is due one month after the end of the grant period.
    - The report must be submitted as an Adobe PDF document electronically to gcipr@acs.org. The report will be shared with the member companies of the Roundtable.
    - The content of the report will be targeted for publication in a peer review technical journal within six months of the conclusion of the research. As a collaborative research project, the paper will be written by the principal investigator and student(s) performing the work, with the Roundtable as co-authors.

**Intellectual Property, Publication Acknowledgement, and Terms of the Grant:**

- The primary purpose of this grant is to publish research to make information publicly available.
- Every patent, United States or foreign, that results from research funded (in part or in its entirety) by the ACS Green Chemistry Institute Pharmaceutical Roundtable Research Grant shall be immediately dedicated to the public, royalty free.

- Each publication prepared in connection with the ACS GCI Pharmaceutical Roundtable Research Grant shall make acknowledgement to the ACS GCI Pharmaceutical Roundtable Research Grant, in the following manner. "Acknowledgement is made to the ACS GCI Pharmaceutical Roundtable Research Grant for support (or partial support) of this research."
- Acceptance of a Roundtable Research Grant will be conditioned upon agreement by the grantee institution that in the event the principal investigator is unable for any reason to conduct the research proposed, the funds, if previously paid by the Roundtable, shall, upon demand, be returned in full to the Roundtable, and further, that in the event the PI is unable for any reason to continue with the research after it has commenced, this grant shall be terminated forthwith and the unexpended and unencumbered balance of any funds theretofore advanced shall be returned to the Roundtable.
- The grantee institution, by acceptance of this grant, provides assurance that support normally provided by the institution for research of the faculty member will not be diminished.
- Applicants may have only one research grant with the ACS GCI Pharmaceutical Roundtable at a time. Current research grant holders may apply for a new grant provided the current grant will be closed by December 31, 2014. In order to close a grant, the required reports must be received and approved by the ACS GCI Pharmaceutical Roundtable.

**For additional information:**
Website: www.acs.org/gcipharmaroundtable
Email: gcipr@acs.org