Role of Academic Science and Technology Centers in Developing Enabling Technologies

Case Study: NSF Center for Selective C-H Functionalization
What is C–H Functionalization?

The Organometallic Chemist's View
“The Holy Grail”

“One “Holy Grail” of C-H activation research, therefore, is not simply to find new C-H activation reactions but to obtain an understanding of them that will allow the development of reagents capable of selective transformations of C-H bonds into more reactive functionalized molecules.”

\[ \text{CH}_4 \rightarrow \text{CH}_3\text{OH} \]

\[ \text{phenyl} \rightarrow \text{phenyl-}X \]

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3-X \]
The Organic Chemists View: Paradigm Shifting Synthetic Strategy

REACTIVE SITES FOR FUNCTIONAL GROUP MODIFICATION

REACTIVE SITES FOR C–H FUNCTIONALIZATION

Major Impact on fine chemical synthesis, sustainable synthetic methods, innovative approaches for pharmaceuticals and high performance materials

C–H Functionalization: Development of the Field
C–H Functionalization: Applications of the Field
Collaborative Beginnings of the CCHF
Phase II of the CCHF
Expanding the CCHF’s Horizons
The Center for Selective C–H Functionalization
Footprint of the CCHF
To leverage the collaborative potential of the Center to Develop technology for Selective C-H Functionalization that will Revolutionize the practice and reshape the Teaching of chemical synthesis, Empowering end users in Materials Science, Fine Chemicals development, and Drug Discovery.
Building Synergy: Weekly Videoconference Meeting
Center Grand Challenges

- Generate a tool-box of effective catalysts and methods for the selective functionalization of C-H bonds.

- Develop selectivity rules for C-H functionalization of complex substrates.

- Revolutionize the strategies used for the synthesis of complex natural products.

- Develop strong alliances with other centers and industrial partners to maximize the application of the C-H functionalization methodologies to the synthesis of pharmaceuticals, agrochemicals and new materials.

- Become the recognized leader in advancing C-H functionalization to impact broadly the logic of organic synthesis.
Streamlined Synthesis Using Sequential C-H Functionalizations

Gang Li (Yu Group)

Jin-Quan Yu - Scripps

Keary Engle (Yu Group)

Hengbin Wang (Davies Group)

Huw Davies - Emory

Hengbin Wang; Gang Li; Keary M. Engle; Jin-Quan Yu; Huw M. L. Davies; J. Am. Chem. Soc. 2013, 135, 6774-6777.
Isolation and Characterization of Rhodium-Carbenoids

John Berry – UW Madison

Kasia Kornecki

Jochen Autschbach
SUNY Buffalo

Mechanistic Models

Vyacheslav Boyarskikh

Felicia Fullilove

Process Optimization

Huw Davies - Emory

Philip Pelphrey

Jørn Hansen

Fred Briones

UV-Vis:

Mass observed by MALDI-MS:
$\text{m/z} = 1533.7$, calc. = 1533.3

+ diazo 0°C
Designing Selective Catalysts for C-H Functionalization

Adrián Varela-Álvarez - Emory
Jamal Musaev - Emory
Clayton Owens - Emory
Simon Blakey - Emory
Huw Davies - Emory

iridium(III) phebox

1.) 0.5 mol % 8, PhCF₃
4Å MS, rt or 45 ºC
2.) DDQ, PhH, rt

96 % 95 % ee
98 % 94 % ee
53 % 95 % ee
CCHF Interactions with Industrial Sponsors

- **Collaborating Partner (CP) ($100,000+)**
  - Broad, all-encompassing non-IP interactions in all Center research and outreach activities.
  - Early communication of research results and outreach activities

- **Collaborating Industrial Affiliate (CIA) ($50,000+)**
  - Focused projects with specific members of the Center for research or outreach.
  - Early communication of research results and outreach activities

- **Industrial Affiliate (IA) ($10,000)**
  - Early communication of research results and outreach activities
Model for Collaborations with Industry

Collaborative Research Engagement (Open)

Connection With Advances

IP Directed Research (Closed)
Benefits: Symposia with the CCHF

Quarterly Virtual Symposia (CP, CIA, IA):
- Interactive Video-Conference
- Dissemination of scientific results and outreach activities
- Interaction with faculty and student CCHF members

Annual Symposium (CP, CIA, IA):
Learn about the science, meet the members, network with the community all face to face in an exciting, enthusiastic and open atmosphere.

Collaborative CCHF/Company Meeting (CP):
Special collaborative one-day symposium with the Center and Industrial partner. Including in-depth discussion with faculty and students.
Benefits: Research Interactions with the CCHF

Monthly Update Newsletter (CP, CIA, IA):
- General News and Outreach Update on Center Activities
- Center calendar and upcoming events

Affiliate Interactions (CIA):
- Focused investigations on specific challenges
- Working with individuals or small teams of Center members

Partner Interactions (CP):
- Broad, all encompassing disclosure of Center activities
- Working on long-term grand challenges
- Collaborative goals and challenges
Benefits: Network and Exchange with the CCHF

**Academic Network:**
- Communicate directly with a network of faculty, postdocs and students from across the United States
- Exposure and interaction on a national scale through scientific and outreach activities

**Interact with Future Scientists**
- Communication with and access to a community of highly-trained graduate and postdoctoral students
- Graduates from the Center will have experience of collaborative, interdisciplinary research programs and learnt the skills required to make these a success
Coordination of Publications with Commercialization of Reagents (Yu with Aldrich)

Jian He; Masayuki Wasa; Kelvin S. L. Chan; Jin-Quan Yu; J. Am. Chem. Soc. 2013, 135, 3387-3390.
Natural Product Synthesis and Late Stage Functionalization (Yu with Baran)

Brandon R. Rosen, Leah R. Simke, Peter S. Thuy-Boun, Darryl D. Dixon, Jin-Quan Yu*, Phil S. Baran*
DOI: 10.1002/anie.201303838.
New Catalysts for Pharmaceutical Process Chemistry (Davies with Bristol-Myers-Squibb)

Discovery and development of a scalable synthesis for the HCV NS5B inhibitor BMS-791325. Presented by Rodeny S. Parsons, BMS. Paper 346, Organic Division, American Chemical Society, National Meeting, New Orleans, April 08, 2013
Discovery and development of a scalable synthesis for the HCV NS5B inhibitor BMS-791325. Presented by Rodeny S. Parsons, BMS. Paper 346, Organic Division, American Chemical Society, National Meeting, New Orleans, April 08, 2013
Applications to Agrochemical Targets (Yu with Syngenta)

Mengchun Ye; Guo-Lin Gao; Andrew J. F. Edmunds; P. A. Worthington; James A. Morris; Jin-Quan Yu; J. Am. Chem. Soc. 2011, 133, 19090-19093.
Diversity Synthesis of Pharmaceutical Targets (Yu with Pfizer)

Hui-Xiong Dai; Antonia F. Stepan; Mark S. Plummer; Yang-Hui Zhang; Jin-Quan Yu; J. Am. Chem. Soc. 2011, 133, 7222-7228.
Conclusion

◆ C-H Functionalization is reaching the stage of maturity for broad commercial application

◆ CCHF offers a collaborative team approach for developing C-H functionalization

◆ Broad collaborations are becoming the driver of modern organic chemistry research

◆ Collaborations between CCHF and industry enhances the rapid development of C-H functionalization

This work was supported by NSF under the CCI Center for Selective C-H Functionalization, CHE-1205646

Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation (NSF)
# Affiliation Benefits Overview

<table>
<thead>
<tr>
<th>Affiliation Type</th>
<th>CP (Collaborating Partner)</th>
<th>CIA (Collaborating Industrial Affiliate)</th>
<th>IA (Industrial Affiliate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affiliation Cost</td>
<td>$100,000+</td>
<td>$50,000+</td>
<td>$10,000</td>
</tr>
<tr>
<td>Association</td>
<td>Logo/Name on Center Posters</td>
<td>Logo/Name on Center Presentations</td>
<td>Logo/Name on Center Website</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sponsorship of Outreach Activities</td>
</tr>
<tr>
<td>Symposia</td>
<td>Quarterly Virtual Symposia</td>
<td>Annual Symposium</td>
<td>Collaborative CCHF/Company Meetings</td>
</tr>
<tr>
<td>Research Interaction</td>
<td>Monthly Internal Update Newsletter</td>
<td>Monthly External Update Newsletter</td>
<td>Discussion on Technical Challenges</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Collaborative Proposal Building</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Advance Notice of Inventions</td>
</tr>
<tr>
<td>Networking &amp; Exchange</td>
<td>Sponsored Fellow Program</td>
<td>Access to online Member Resumes</td>
<td>Facilitated Interviews</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Contact with Center &amp; Affiliate Network</td>
</tr>
</tbody>
</table>

- **Broad, all-encompassing non-IP interactions in all Center research and outreach activities**
- **Focused interactions with specific members of the Center for research or outreach.**
- **Communication of research results and outreach activities**

Additional benefits/interactions may be mutually agreed upon.