



UNI

THE PETROLEUM RESEARCH FUND UNDERGRADUATE NEW INVESTIGATOR PROPOSAL

(Please refer to statement of eligibility, terms, and conditions.)

HIGHLY CONFIDENTIAL

This proposal is intended for review exclusively by ACS PRF staff, members of the PRF Committee, and outside reviewers officially asked to furnish scientific comments. It may not be transmitted to other parties, copied, or retained for future reference; please destroy after use.

Allegra L. Liberman-Martin

August 01, 2018

(Principal Investigator)

(Date of First Faculty Appointment)

Chemistry and Biochemistry

Chapman University

Orange

CA

(Department)

(Institution)

(City)

(State)

Title of Proposed Research:

Carbodiphosphanes as Organocatalysts for Carbodiimide and Isocyanate Reduction

The ACS Petroleum Research Fund does not tolerate scientific misconduct. Scientific misconduct includes, but is not limited to, fabrication, falsification, and plagiarism. Instances of alleged or suspected scientific misconduct will be referred to the PRF Committee for investigation. Upon a determination of scientific misconduct, the PRF Committee may, in its discretion, take any actions it deems appropriate. Such actions may include: disqualifying proposals from consideration; disqualifying individuals or institutions from submitting future proposals; revoking grant awards; contacting appropriate Officers of the relevant institution(s), such as the Dean, and/or Department Head of the investigator(s); and other such actions that the PRF Committee feels are appropriate.

The ACS Petroleum Research Fund reserves the right to scan proposals for plagiarism.

By signing below, we acknowledge that we have read and understand this scientific misconduct policy.

In addition, we confirm that, should this proposal be funded, the proposed budget will become the approved grant budget and funds will be spent according to the budget amounts and categories approved by ACS PRF. Any revisions to the approved budget require prior approval from an ACS PRF Program Manager.

Principal Investigator:

[Handwritten Signature]

(Signature)

March 12, 2020

(Date)

Officer of the Institution Endorsing the Proposal:

[Handwritten Signature: Molly McCarty]

(Signature)

Research Administrator

(Title)

3/11/2020

(Date)

PROPOSED BUDGET — UNDERGRADUATE NEW INVESTIGATOR GRANT

Amount: \$55,000 for two grant years. Although some budget flexibility can be allowed, *with prior approval*, after a grant has been awarded, an outline of the projected use of the funds will aid in the evaluation of the proposal. Shifts in budget category allocations, consistent with the terms and conditions outlined on page v, and time extensions without the commitment of additional funds may be arranged *with prior approval*. Funds not expended in one budget year may be carried forward into the next in the same category. **Do not add any categories to this budget page; the listed categories are the only expenditures approved.**

Each period must end on August 31 and be at least twelve months in duration.
A starting date earlier than September 1 will result in a first budget period longer than twelve months.

For the Periods

Approved budget categories:	June 1, 2021 to Aug. 31, 2022	Sept. 1, 2022 to Aug. 31, 2023
1. Salaries/stipends (includes benefits):		
a. Principal Investigator (maximum: \$8,000/ grant year)	<u>\$7,207 + \$793 = \$8,000</u>	<u>\$7,207 + \$793 = \$8,000</u>
b. Undergraduate Student(s)*	<u>\$17,600 + \$880 = \$18,480</u>	<u>\$6,3000 + \$300 = \$6,300</u>
c. Master's Student(s)	<u>0</u>	<u>0</u>
2. Expendable Supplies and Services i.e., Chemicals, Glassware, Analyses, etc.	<u>\$6,110</u>	<u>\$6,110</u>
3. Capital Equipment (max: \$5,000; see instructions)	<u>0</u>	<u>0</u>
4. Travel (conference) (maximum: \$2,000/ grant year)	<u>\$1,000</u>	<u>\$1,000</u>
5. Field work:		
a. Principal Investigator	<u>0</u>	<u>0</u>
b. Students	<u>0</u>	<u>0</u>
ANNUAL TOTALS	<u>\$33,590</u>	<u>\$21,410</u>

TOTAL AMOUNT

\$55,000*

Principal Investigator: _____



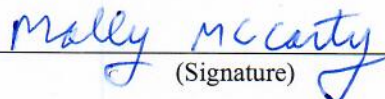
(Signature)

March 12, 2020

(Date)

Officer of the Institution

Endorsing the Proposal: _____



(Signature)

Research Administrator

(Title)

3/11/2020

(Date)

Grantee Institution: _____

Chapman University

I. *Because students at U.S. military academies are prevented from receiving research stipends or additional support above their scholarships, faculty at these institutions may submit UNI proposals with a budget reduced by the recommended 40% student support (i.e., total UNI budget of \$33,000).

I. BUDGET JUSTIFICATION

Describe the intended use of grant funds including number and level of students receiving support. If field work is budgeted, describe the purpose and location, and the number of students involved. Additionally, specify how those funds will be allocated, *e.g.*, for transportation, lodging, etc.

If capital equipment is requested, provide a detailed description of the proposed equipment and the need it fulfills in your research; also describe any matching funds that are to be obtained.

(1) Salaries/stipends

Funding is requested for PI Liberman-Martin and undergraduate research assistants. The \$8,000 per summer during 2022 and 2023 will cover the PI's salary, including 11% for fringe benefits. Undergraduate research assistants will work each summer for 40 hours per week for 10 weeks. One undergraduate will work from June–August, 2021 at \$14/hour, two undergraduates will work from June–August, 2022 at \$15/hour, and one undergraduate will work from June–August, 2023 at \$15/hour. These wages reflect the California minimum wage rate in effect each summer. An additional 5% is included for undergraduate research assistant fringe benefits.

(2) Expendable Supplies and Services

The PI requests \$6,110 in lab supplies and consumables per year. Laboratory consumables include chemicals (reagents, catalyst precursors), glassware (J. Young tubes and Schlenk tubes), and solvents (bulk and deuterated NMR solvents). Services will entail combustion analysis, a resource that is not available on campus.

(3) Travel

A small portion of the grant, \$1,000 per year, will be used for student travel to conferences.

II. EDUCATION AND EXPERIENCE

- a. Indicate all academic degrees, **when** and where received, and Ph.D. thesis title **and supervisor**. List postdoctoral appointment(s) **and supervisor(s)**, if appropriate. List **current and previous positions**, in chronological order; significant honors and awards; and other pertinent biographical information.

Bachelor of Arts in Chemistry, May 2010, Scripps College

Honors in Chemistry, *summa cum laude*

Thesis Supervisor: Prof. Nancy B. S. Williams

Thesis Title: *Aryl Orientation Preferences during Reductive Elimination from Platinum Complexes*

Doctor of Philosophy in Chemistry, December 2015, University of California, Berkeley

Thesis Supervisors: Prof. T. Don Tilley and Robert G. Bergman

Thesis Title: *Lewis Acid Mediated Reactions: Electronic Modification of Platinum Complexes and Metal-Free Catalysis*

Resnick Sustainability Institute Postdoctoral Fellow, March 2016 – July 2018, California Institute of Technology

Research Supervisor: Prof. Robert H. Grubbs

Project: *Investigation of Brush Polymers as Stimuli-Responsive Photonic Crystals*

Assistant Professor of Chemistry and Biochemistry, Chapman University

August 1, 2018 to present

Honors and Awards:

- 2017 Outstanding Poster Award, Division of Polymer Chemistry, 253rd American Chemical Society National Meeting
- 2016 Resnick Sustainability Institute Postdoctoral Fellowship
- 2016 Benjamin Boussett Award, College of Chemistry, University of California Berkeley (award for exemplifying commitment to social or environmental change)
- 2010 Phi Beta Kappa
- 2010 Barbara McClintock Award for Best Senior Thesis in the Sciences, Scripps College
- 2010 ACS Division of Inorganic Chemistry Undergraduate Award, Scripps College

- b. Do you currently hold a tenure-track position? Yes. If not, please contact a PRF Program Manager. Proposals from faculty in non-tenure-track positions must include a letter from your department chair verifying you meet all three ACS PRF eligibility criteria (see pages i-ii).

III. STATEMENT OF OPPORTUNITY TO CONDUCT RESEARCH AT GRANTEE INSTITUTION

- a. Highest academic degree awarded to students in your department: Bachelor of Science
- b. Available facilities - space, equipment, and supplies.

Research Lab:

- 450 square feet of research space
- Three 4-foot-wide fume hoods, containing three custom-made Schlenk lines for air-free experiments
- MBraun LabstarPro glove box (four gloves): outfitted with a cold well, feedthrough for vacuum, purge functionality, and freezer for the synthesis of air- and moisture-sensitive compounds
- JCMeyer solvent purification system: dispenses six anhydrous and degassed organic solvents
- TOSOH gel permeation chromatography (GPC) instrument with Wyatt 18 angle Multi-Angle Light Scattering (MALS) detector for polymer characterization
- Two rotary evaporators
- Group computer (with ChemDraw, SciFinder, and MestreNova software)

Major Shared Instrumentation:

- 400 MHz Bruker NMR spectrometer with variable temperature and heteronuclear capabilities
- Bruker Metaljet X-ray diffractometer (housed at Chapman's Pharmacy School)
- Agilent GC-MS, Bruker MALDI-TOF mass spectrometer (at Pharmacy School), Bruker ESI-QTOF mass spectrometer (at Pharmacy School)
- Attenuated-total reflectance (ATR) IR spectrometers (2)
- Agilent Cary 60 UV-Vis spectrophotometer
- -30 °C and -80 °C freezers

- c. Teaching duties - list the courses you are expected to teach in a typical year and give contact hours per week for lectures, recitations, and laboratory.

Fall Semester:

Organic Chemistry I (lecture): 3h/week

Advanced Organic Chemistry (lecture): 3h/week

Spring Semester:

Organic Chemistry II (lecture): 3h/week

Organic Chemistry II (laboratory): 4h/week

Percentage of time devoted to research during academic year: 40%

Percentage of time devoted to research during summer: 100% Please describe any factors that would significantly detract from available summer research time.

IV. CURRENT AND PENDING SUPPORT

- a. List any active research grants or other current financial support received for research. Give titles, dollar amounts (*annual direct costs*; if more than one PI, indicate only your share of the granted amount), sources, time periods of awards, and *relationship to this proposal*. Use separate page if necessary; indicate “none” if applicable.

Title: Start-up support from Chapman University

Dollar amount: \$260,000

Source: Chapman University

Time period: August 2018–June 2021

Relationship to this proposal: The start-up funds from Chapman University have funded the setup of my research laboratory and the preliminary results presented in this proposal. These funds also cover a range of other projects in my research group.

Chapman University Faculty Opportunity Fund Grant

Title: Metal-Free Reduction of Carbon Dioxide by a Carbodiphosphorane Organocatalyst

Dollar amount: \$15,000

Source: Chapman University

Time period: June 2019–June 2020

Relationship to this proposal: The Chapman University Faculty Opportunity Fund Grant provides seed funds to generate preliminary results within a new area of research. The research funded by this program covered a project investigating the ability of carbodiphosphoranes to catalyze carbon dioxide reduction. This research is related to, but not the same as, the proposed research involving carbodiimide and isocyanate reduction by carbodiphosphorane catalysts.

- b. List any other research grant applications pending. Give titles, dollar amounts requested (*annual direct costs*), sources, *relationship to this proposal*, and date of funding decision for each application. Use separate page if necessary; indicate “none” if applicable.

None

- c. Describe any start-up support or funding. Use separate page if necessary; indicate “none” if applicable.

Title: Start-up support from Chapman University

Dollar amount: \$260,000

Source: Chapman University

Time period: August 2018–June 2021

Relationship to this proposal: The start-up funds from Chapman University have funded the setup of my research laboratory and cover a range of projects in my research group.

In addition to these start-up funds, Chapman University purchased the following shared equipment in support of my research program when I joined the faculty: solvent purification system (\$35,000), 400 MHz NMR spectrometer (\$380,000), and a Wyatt Multi-Angle Light Scattering Detector (MALS) accessory (\$77,000) for polymer characterization.

V. PUBLICATIONS

List all research publications and presentations. Include titles, co-authors (underline student co-authors in both listings), and literature references. Use separate page(s) if necessary.

Publications

14. Chu, C. K.; Lin, T.-P.; Shao, H.; **Lieberman-Martin, A. L.**; Liu, P.; Grubbs, R. H. Disentangling Ligand Effects on Metathesis Catalyst Activity: Experimental and Computational Studies of Ruthenium–Aminophosphine Complexes. *J. Am. Chem. Soc.* **2018**, *140*, 5634–5643.
13. **Lieberman-Martin, A. L.**; Grubbs, R. H. Ruthenium Olefin Metathesis Catalysts Featuring a Labile Carbodicarbene Ligand. *Organometallics* **2017**, *36*, 4091–4094.
12. Chang, A. B.; Lin, T.-P.; Thompson, N. B.; Luo, S.-X.; **Lieberman-Martin, A. L.**; Chen, H.-Y.; Lee, B.; Grubbs, R. H. Design, Synthesis, and Self-Assembly of Polymers with Tailored Graft Distributions. *J. Am. Chem. Soc.* **2017**, *139*, 17683–17693.
11. Suslick, B. A.; **Lieberman-Martin, A. L.**; Wambach, T. C.; Tilley, T. D. Olefin Hydroarylation Catalyzed by (Pyridyl-Indolate)Pt(II) Complexes: Catalytic Efficiencies and Mechanistic Aspects, *ACS Catal.*, **2017**, *7*, 4313–4322.
10. **Lieberman-Martin, A. L.**; Chu, C. K.; Grubbs, R. H. Application of Bottlebrush Block Copolymers as Photonic Crystals. *Macromol. Rapid Commun.* (special issue on “Polymers and Light”), **2017**, DOI: 10.1002/marc.201700058.
9. Lin, T.-P.; Chang, A. B.; Chen, H.-Y.; **Lieberman-Martin, A. L.**; Bates, C. M.; Voegtle, M.; Bauer, C. A.; Grubbs, R. H. Control of Grafting Density and Distribution in Graft Polymers by Living Ring-Opening Metathesis Copolymerization. *J. Am. Chem. Soc.* **2017**, *139*, 3896–3903.
8. Lipke, M. C.; **Lieberman-Martin, A. L.**; Tilley, T. D. Electrophilic Activation of Silicon–Hydrogen Bonds in Catalytic Hydrosilations. *Angew. Chem., Int. Ed.* **2017**, *56*, 2260–2294.

7. **Lieberman-Martin, A. L.**; Levine, D. S.; Ziegler, M. S.; Bergman, R. G.; Tilley, T. D. Lewis Acid-Base Interactions between Platinum(II) Diaryl Complexes and Bis(perfluorophenyl)zinc: Strongly Accelerated Reductive Elimination Induced by a Z-Type Ligand. *Chem. Commun.* **2016**, 52, 7039–7042.
6. Lipke, M. C.; **Lieberman-Martin, A. L.**; Tilley, T. D. Significant Cooperativity Between Ruthenium and Silicon in Catalytic Transformations of an Isocyanide. *J. Am. Chem. Soc.* **2016**, 138, 9704–9713.
5. **Lieberman-Martin, A. L.**; Ziegler, M. S.; DiPasquale, A. G.; Bergman, R. G.; Tilley, T. D. Functionalization of an Iridium–Diamidocarbene Complex by Ligand-Based Reactions with Titanocene and Zirconocene Sources. *Polyhedron* (special issue dedicated to Malcolm L. H. Green) **2016**, 116, 111–115.
4. **Lieberman-Martin, A. L.**; Levine, D. S.; Liu, W.; Bergman, R. G.; Tilley, T. D. Biaryl Reductive Elimination Is Dramatically Accelerated by Remote Lewis Acid Binding to a 2,2'-Bipyrimidyl–Platinum Complex: Evidence for a Bidentate Ligand Dissociation Mechanism. *Organometallics* **2016**, 35, 1064–1069.
3. **Lieberman-Martin, A. L.**; Bergman, R. G.; Tilley, T. D. Lewis Acidity of Bis(perfluorocatecholato)silane: Aldehyde Hydrosilylation Catalyzed by a Neutral Silicon Compound. *J. Am. Chem. Soc.* **2015**, 137, 5328–5331.
2. **Lieberman-Martin, A. L.**; Bergman, R. G.; Tilley, T. D. A Remote Lewis Acid Trigger Dramatically Accelerates Biaryl Reductive Elimination from a Platinum Complex. *J. Am. Chem. Soc.* **2013**, 135, 9612–9615.
1. Erupe, M. E.; **Lieberman-Martin, A. L.**; Silva, P. J.; Malloy, Q. G. J.; Yonis, N.; Crocker, D. R.; Purvis-Roberts, K. L. Determination of Methylamines & Trimethylamine-N-oxide in Particulate Matter by Non-suppressed Ion Chromatography. *J. Chromatogr. A.* **2010**, 1217, 2070–2073.

Presentations (presenters in bold; undergraduate students underlined)

Fleener, C. R.; Chang, D. K.; Lieberman-Martin, A. L. Exploring a Carbodiphosphorane Catalyst in Ketone Hydroboration. Student Scholar Symposium, Chapman University, Orange, CA, December 2019.

Naumann, R. A.; Lieberman-Martin, A. L. Biodegradable Plastic Synthesis Using Metal-Free Catalysis. Student Scholar Symposium, Chapman University, Orange, CA, December 2019.

Chang, D. K.; Fleener, C. R.; Lieberman-Martin, A. L. Carbodiphosphorane-Catalyzed Hydroboration Reactions. 258th ACS National Meeting and Exposition, San Diego, CA, August 2019. (poster)

Chang, D. K.; Fleener, C. R.; Lieberman-Martin, A. L. Hydroboration Reactions Using a Carbodiphosphorane Catalyst. SoCal Undergraduate Chemistry Research Symposium, Irvine, CA, August 2019. (poster)

Lieberman-Martin, A. L.; **Chang, D. K.**; **Fleener, C. R.** Hydroboration by a Cyclic Carbodiphosphorane Organocatalyst. Organometallics Gordon Research Conference, Newport, RI, July 2019. (poster)

Lieberman-Martin, A. L. Metal-Free Catalysis for Organic and Polymer Synthesis. Chapman University Summer Undergraduate Research Fellowship (SURF) Seminar Series. Orange, CA, July 2019.

Liberman-Martin, A. L.; Grubbs, R. H. Ruthenium Olefin Metathesis Catalysts Featuring Carbodicarbene and Carbodiphosphorane Ligands. Organometallics Gordon Research Conference, Newport, RI, July 2018. (poster)

Liberman-Martin, A. L. Stimuli-Responsive Molecules: From Inorganic Complexes to Light-Reflecting Polymers. Chemistry Department Seminar, Reed College, Portland, OR, September 2017.

Liberman-Martin, A. L.; Chu, C. K.; Grubbs, R. H. Synthesis and Self-Assembly of Brush Block Copolymers with Low T_g Side Chains. 254th American Chemical Society National Meeting, Washington, DC, August 2017.

Liberman-Martin, A. L.; Chu, C. K.; Chang, A. B.; Grubbs, R. H. Self-Assembly of Brush Block Copolymer Photonic Crystals Featuring Low T_g Side Chains. 253rd American Chemical Society National Meeting, San Francisco, CA, April 2017. (poster)

Liberman-Martin, A. L. Side Chain Design in Brush Block Copolymer Photonic Crystals. Resnick Foundation Seminar, California Institute of Technology, Pasadena, CA, March 2017.

Liberman-Martin, A. L.; Bergman, R. G.; Tilley, T. D. Activation of Platinum Complexes by Ligand-Based Reactions with Lewis Acids. Organometallics Gordon Research Conference and Seminar, Newport, RI, July 2015. (poster at GRC, speaker at GRS)

Liberman-Martin, A. L.; Bergman, R. G.; Tilley, T. D. Aldehyde Hydrosilylation Catalyzed by a Neutral Bis(perfluorocatecholato)silicon Compound. 46th Silicon Symposium, Davis, CA, June 2015.

Liberman-Martin, A. L. Activation of Platinum Complexes by Ligand-Based Reactions with Lewis Acids. University of California, Berkeley, Berkeley, CA, February 2015. *Invited seminar for prospective graduate students.

Liberman-Martin, A. L. Activation of Platinum Complexes by Ligand-Based Reactions with Lewis Acids. Inorganic Division Seminar, University of Washington, Seattle, WA, January 2015.

Liberman-Martin, A. L.; Bergman, R. G.; Tilley, T. D. Remote Triggers for the Activation of Unreactive Bonds by Late Metal Complexes. 248th American Chemical Society National Meeting, San Francisco, CA, August 2014.

Liberman-Martin, A. L.; Bergman, R. G.; Tilley, T. D. Platinum Complexes Activated by Ligand-Based Reactions with Lewis Acids. 245th American Chemical Society National Meeting, New Orleans, LA, April 2013.

VI. SAFETY

Principal Investigators must describe any significant risks or hazards that may be encountered in the proposed work, and how these risks or hazards would be mitigated.

All students will complete online courses in basic laboratory safety (overseen by a full-time Lab Operations & Safety Director within Schmid College of Science and Technology at Chapman University), as well as receive hands-on fire extinguisher training. All students are provided copies of group standard operating procedures (SOPs) for basic laboratory safety, Schlenk line use, cryogen handling, and pyrophorics handling. The PI goes over these documents with each student and supervises students individually until proficiency in each area is achieved. If pyrophoric reagents are required, the PI oversees the use of these chemicals regardless of the experience level of the student.

All necessary personal protective equipment (PPE) is supplied to researchers by the PI, including safety glasses, chemical splash goggles, chemical resistant gloves, and flame-retardant lab coats.

The proposed project uses synthetic methods that require the use of pyrophoric, potentially carcinogenic, caustic, and corrosive materials. The strong base benzyl potassium is used in the deprotonation of the carbodiphosphorane. This compound is used in a glovebox under the supervision of the PI. All students follow standard operating procedures (SOPs) in quenching trace amounts of benzyl potassium while being supervised by the PI.

As in all synthetic laboratories, all new compounds with unknown biological properties are treated with the utmost care. The vast majority of compounds are prepared in the glovebox under a nitrogen atmosphere, which provides an additional level of security in limiting the chemical exposure of the students and PI.

VII. SUGGESTED REVIEWERS

Provide the names and addresses (including email) of at least six suggested reviewers who are experts in the field of the proposed research. Do not include former research mentors, students, collaborators, or colleagues at your current or former institutions. It is suggested that you include, but are not limited to, the names of experts residing in the United States, as well as faculty at primarily undergraduate institutions. Also, please do not list names of any reviewers whom you have suggested in any proposal previously submitted to ACS PRF **within the past four years**. Include the first name, middle initial (if any), academic institution, department, and *email address* of all suggested reviewers.

NOTE: This information is also entered as part of the online application, on the proposal submission website.

Professor Christopher R. Graves
Swarthmore College
Department of Chemistry and Biochemistry
500 College Ave., Swarthmore, PA 19081
Email: cgraves1@swarthmore.edu

Professor C. Wade Downey
University of Richmond
Department of Chemistry
C-311 Gottwald Center for the Sciences, Richmond, VA 23173
Email: wdowney@richmond.edu

Professor Todd W. Hudnall
Texas State University
Department of Chemistry and Biochemistry
601 University Dr., San Marcos, TX 78666
Email: th40@txstate.edu

Professor Hosea M. Nelson
University of California, Los Angeles
Department of Chemistry & Biochemistry
607 Charles E. Young Drive East, Los Angeles, CA 90095
Email: hosea@chem.ucla.edu

Professor Rory Waterman
Department of Chemistry
Discovery Hall, 82 University Place, Burlington, VT 05405
Email: rory.waterman@uvm.edu

Professor Vincent Lavallo
Department of Chemistry
501 Big Springs Road, Riverside, CA 92521
Email: vincent.lavallo@ucr.edu

VIII. COLLABORATIONS

If you will be collaborating with other scientists in the performance of the research described in this proposal, identify the collaborators and briefly indicate the nature of the collaboration. If any of these collaborators are current ACS PRF grantees or applicants, discuss the relationship between this proposal and the collaborator's ACS PRF project. A letter from the collaborator(s), confirming the extent and nature of the collaboration, should be added to the application.

I do not have any currently planned collaborations for the proposed project.

October 2020

IX. SCIENTIFIC EDUCATIONAL IMPACT (Limited to one page; 12-point font)

Provide a brief description of how your mentoring of students will impact scientific education in your institution and department. For example, you might discuss the level of student required to do the work, (i.e., freshman, sophomore, etc.); what role they will play in carrying out the proposed research in terms of intellectual and time commitment; and how the research carried out by the students will be a part of their degree requirements and departmental goals.

The top priority of my research group is the training and education of undergraduate researchers. All projects in the Liberman-Martin group focus on sustainable catalysis, and students learn to contextualize their work from the perspective of broader global energy and environmental challenges. Students at all stages of their undergraduate education join the research group; the group currently consists of five sophomores and two juniors, along with a teacher-scholar post-doctoral fellow, Dr. Zachary Thammavongsy, and a research assistant, Daniel Chang (Chapman '19). All undergraduate researchers are trained directly by the PI in both experimental techniques and safety.

To empower undergraduate researchers to make new scientific discoveries, projects are structured such that each student takes intellectual ownership of a small piece of a given project. This includes performing literature searches, planning and executing experiments, analyzing results, and troubleshooting for their project. I hold structured weekly group meetings throughout the calendar year, at which students present their latest results and analyze literature articles. To develop their academic portfolios and science communication skills, I encourage students to apply for relevant awards and present results at regional and national meetings. I view the problem-solving and communication skills gained in the research laboratory as valuable and transferable, regardless of whether or not students ultimately pursue a career in the chemical sciences.

The Liberman-Martin Group is an interdisciplinary main group chemistry group focused on mechanistic studies and metal-free catalysis. Our work is at the interface of organic, inorganic, and physical chemistry, which provides undergraduate researchers with broad exposure to several sub-disciplines of chemistry. The group is the only research group in Chapman that focuses on synthetic chemistry and homogeneous catalysis. The physical lab space is outfitted with all necessary equipment to train undergraduates in air-free synthesis techniques, including three Schlenk lines, a double glove box, and a solvent purification system. We have access to Chapman's NMR, X-Ray, and mass spectrometry facilities, which are free of charge for internal users.

Chapman University is a medium sized, private liberal arts college located in Southern California. There is a strong culture promoting student-centered learning at Chapman, which has a university mission statement of providing personalized education. The Chemistry and Biochemistry Unit at Chapman is located within Schmid College of Science and Technology, which has recently undertaken major enhancements in research infrastructure in conjunction with the opening of the new 140,000 square foot Keck Science and Technology Center in Summer 2018. The combined number of Chemistry and Biochemistry graduates fluctuates between 20-30 per year, with the total number of declared Chemistry and Biochemistry majors being approximately 90-110 at any given time. There is a strong research culture within the Chemistry and Biochemistry Unit at Chapman, and all Chemistry and Biochemistry majors complete a senior year research Capstone project as a part of their graduation requirement. Students conduct research for 3-9 hours per week during the academic year for credit and work 40 hours per week during the summer. Chapman University offers several forms of grants to students and faculty to support research, including \$1,000 student grants for research supplies, \$4,000 student summer research fellowships, and \$15,000 grants to faculty to develop new research directions.

Carbodiphosphoranes as Organocatalysts for Carbodiimide and Isocyanate Reduction

Abstract

This proposal details the use of carbodiphosphoranes as catalysts for the hydroboration of carbodiimide and isocyanate substrates. Nitrogen-containing compounds are prevalent in pharmaceutical and agrochemical applications, and the development of catalytic C=N reduction methods could improve the sustainability, efficiency, and safety of industrial processes. Carbodiimides and isocyanates are petroleum-derived compounds that are particularly challenging substrates for hydroboration catalysis, as they can undergo either single or double hydroboration. The monohydroboration process for these substrates is an appealing route to synthetically valuable formamidine and formamide species. The nucleophilic catalysts we will study are carbodiphosphoranes, which feature two phosphorus centers flanking a two-coordinate carbon that is formally zerovalent and possesses two lone pairs. As a result of their exceptionally strong donor properties, there is significant interest in the use of carbodiphosphoranes as ligands for transition metals; however, to our knowledge, there are no previous reports using carbodiphosphoranes as nucleophilic organocatalysts. We will investigate the substrate scope of carbodiimide and isocyanate hydroboration along with the mechanisms for catalysis. The mechanistic studies of hydroboration catalysis and broader experiments to experimentally measure the steric and electronic properties of carbodiphosphoranes proposed herein will serve as a reference for the rational development of new organocatalyzed reactions. This investigation, which will be performed in collaboration with undergraduate researchers, will uncover the catalytic potential of carbodiphosphoranes as well as provide new methods to functionalize commodity chemicals that are derived from petrochemical sources.

Background and Significance

Nitrogen-containing molecules are important in pharmaceutical, agrochemical, and materials chemistry applications, which creates an ever-increasing demand for sustainable methods to synthesize nitrogen-containing organic compounds.¹ An appealing synthetic route to amines is through the reduction of C=N bonds.² Stoichiometric methods to reduce C=N bonds often involve stoichiometric quantities of harsh reducing agents, such as LiAlH₄ or NaBH₄.^{3,4} Catalytic C=N reduction reactions can provide improved atom economy and decrease the amount of waste generated in the synthesis of nitrogen-containing compounds.

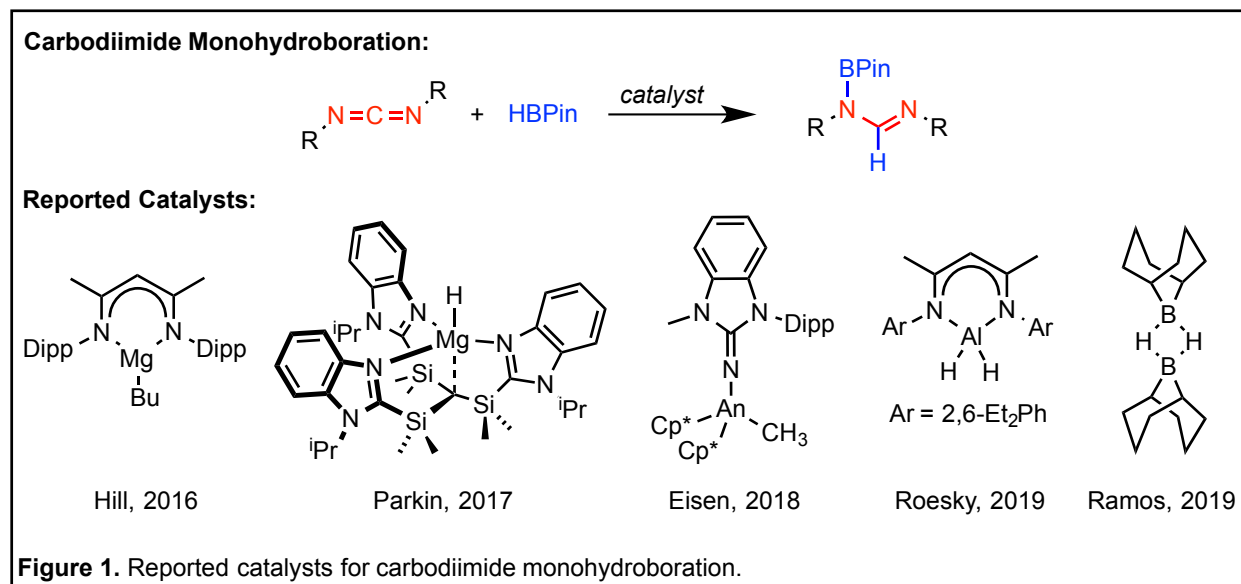
Within the realm of catalytic C=N reduction, methods for imine reduction have been most widely developed. While precious-metal catalysts were among the first reported catalysts for imine hydrogenation,⁵ there have been significant recent advances developing alternative catalysts featuring non-precious elements.^{6,7} To complement hydrogenation methods, imine hydroboration has recently emerged as a growing area of research that takes advantage of borane reagents that can be used under mild reaction conditions without the need for high-pressure apparatus.⁸⁻¹¹

Most examples of catalytic C=N hydroboration catalysis feature substrates with a single polar unsaturated bond, such as imine reagents. In comparison, the catalytic hydroboration of nitrogen-containing heterocumulenes remains less widely developed. Both carbodiimides (RN=C=NR) and isocyanates (RN=C=O) are versatile classes of petroleum-derived feedstocks that are widely available;^{12,13} however, there are limited catalytic reduction methods reported for these substrates. Mono-reduction of carbodiimides and isocyanates is a route to formamidine and formamide products, which are important units in biologically active compounds with bactericidal, fungicidal, and insecticidal properties.¹⁴⁻¹⁷ Development of efficient and selective catalytic

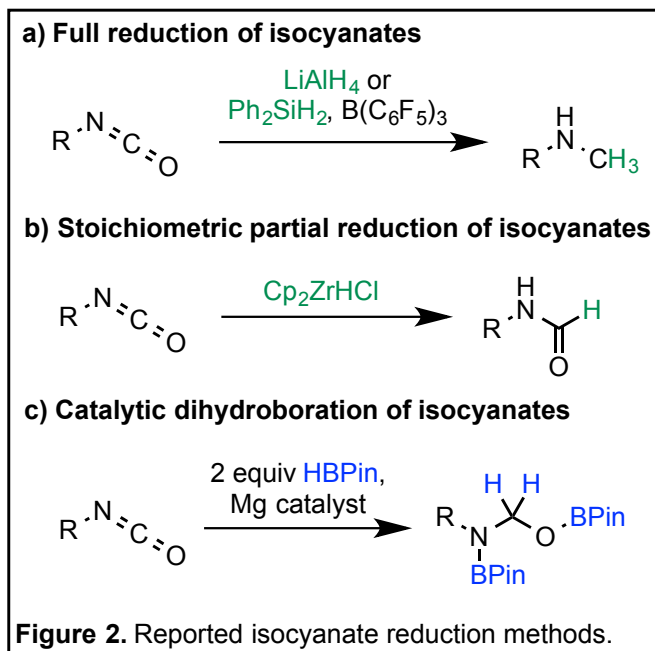
processes for carbodiimide and isocyanate reduction could enable the more sustainable synthesis of nitrogen-containing molecules.

Challenges in the Field

The heterocumulene skeleton of carbodiimides and isocyanates contains two polar double bonds. This poses a challenge for selective reduction, as both single and double reductions are possible. In the absence of a catalyst, treatment of carbodiimides with 9-borabicyclo[3.3.1]nonane (9-BBN) under harsh conditions (160 °C) results in a mixture of single and doubly reduced amidinate and bis(boryl)aminal products.¹⁸ There are a limited number of reported catalysts for the selective monohydroboration of carbodiimides to *N*-borylformamidines (**Figure 1**).^{19–24} Notably, none of the existing catalysts are nucleophilic organocatalysts. This leaves significant room for discovery of new carbodiimide hydroboration catalysts that could operate by alternative reaction mechanisms and could potentially improve reaction efficiency or functional group tolerance.



In comparison, selective methods for isocyanate reduction remain even more scarce (**Figure 2**). Isocyanate reduction with LiAlH_4 or other powerful reducing agents such as NaBH_4/TFA or $\text{Ph}_2\text{SiH}_2/\text{B}(\text{C}_6\text{F}_5)_3$ results in full reduction to *N*-methylamine products.^{25,26} The selective partial reduction of isocyanates to formamides has been accomplished using

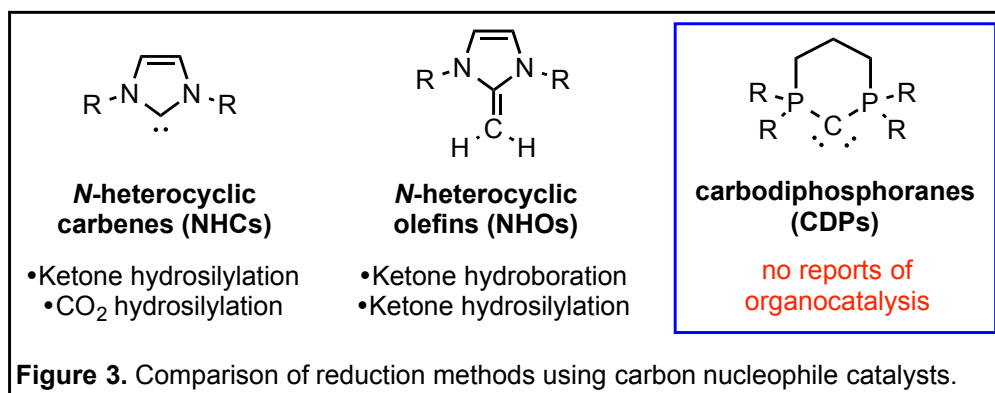


stoichiometric quantities of Schwartz's reagent, Cp_2ZrHCl .²⁷ In the realm of catalytic reduction methods, two recent articles have demonstrated the magnesium-catalyzed dihydroboration of isocyanates to form *N,O*-bis(boryl)hemiaminal species.^{28,29} *To our knowledge, there are no reported methods for the catalytic monohydroboration of isocyanates.* Development of selective isocyanate monohydroboration methods would provide a catalytic route to formamides from readily available isocyanates.

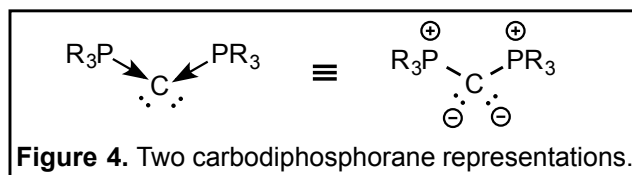
Proposed Catalyst Innovation

This proposal describes the use of carbodiphosphoranes as novel nucleophilic catalysts for hydroboration catalysis. There has been significant recent interest in the development of carbon nucleophiles as organocatalysts (**Figure 3**). Most prominently, *N*-heterocyclic carbenes (NHCs) have emerged as widely used organocatalysts for a range of transformations.³⁰ Within the context of reductive catalysis, NHCs are known to catalyze both ketone and carbon dioxide hydrosilylation.^{31–34} Recently, the catalytic activity of *N*-heterocyclic olefins (NHOs) has been demonstrated in ketone hydroboration and hydrosilylation reactions.^{35,36} The catalytic activity of

NHOs is attributed to reactivity at the exocyclic α -carbon, which is rendered strongly nucleophilic due to the strong polarization of the exocyclic C=C double bond.³⁷



Carbodiphosphoranes constitute an interesting class of molecules featuring two-coordinate carbon that is formally zerovalent and possesses two lone pairs (**Figure 4**).^{38,39} As a result, the central carbon of the carbodiphosphorane framework is strongly nucleophilic. There has been significant interest in carbodiphosphoranes as ligands for transition metal complexes,^{40–46} as carbodiphosphoranes are more strongly donating than *N*-heterocyclic carbene ligands based on Tolman electronic parameters.⁴⁷



In spite of the rich coordination chemistry of carbodiphosphoranes, *to our knowledge, there are no previous reports using carbodiphosphoranes as organocatalysts.* We believe this represents an opportunity to investigate the catalytic potential of these overlooked compounds and to gain deeper insight into their nucleophilic properties. Based on precedent for reductive catalysis by nucleophilic NHCs and NHOs, *we hypothesize that the exceptionally strong donor properties of carbodiphosphoranes will render them highly active as nucleophilic organocatalysts.* This proposal describes synthetic and mechanistic studies of carbodiimide and isocyanate hydroboration catalyzed by carbodiphosphoranes.

Specific Aims

Aim 1. Carbodiphosphorane-Catalyzed Carbodiimide Hydroboration. We will synthesize prototypical cyclic and acyclic carbodiphosphoranes and evaluate them as nucleophilic catalysts. Hydroboration of a series of carbodiimide substrates will be investigated to provide insight into the steric and electronic constraints for catalysis. Mechanistic studies will determine if hydroboration proceeds through either a carbodiphosphorane–carbodiimide or a carbodiphosphorane–borane adduct.

Aim 2. Carbodiphosphorane-Catalyzed Isocyanate Hydroboration. Cyclic and acyclic carbodiphosphorane catalysts will be compared in isocyanate hydroboration reactions. Stoichiometric experiments of carbodiphosphoranes with alkyl and aryl isocyanates will be performed along with kinetics experiments to examine the isocyanate hydroboration mechanism.

Aim 3: Comparison of Carbodiphosphorane Structures to Optimize Catalyst Activity. Four alkyl/aryl carbodiphosphoranes have been selected for in-depth comparison, including two acyclic and two cyclic structures. We will characterize and parametrize the steric and electronic properties of these four carbodiphosphoranes to establish structure-reactivity relationships for hydroboration catalysis.

Training and Development of Undergraduate Student Researchers. Infused in every stage of the proposed research is the involvement of undergraduate student researchers. The Chapman undergraduates that participate in the proposed project will receive training in a diverse skill set, including laboratory techniques, best practices for laboratory notebook documentation, and experience presenting their research to both the Chapman community and at national conferences.

Aim 1. Carbodiphosphorane-Catalyzed Carbodiimide Hydroboration

Aim 1.1 Carbodiphosphorane Selection and Synthesis

To make the proposed project accessible for undergraduate researchers, initial targets for carbodiphosphorane catalysts were selected that (i) can be synthesized from commercially available precursors in two reaction steps, and (ii) are indefinitely stable when stored as solids under inert atmosphere. Two carbodiphosphoranes that meet these criteria are the acyclic and cyclic carbodiphosphorane structures in

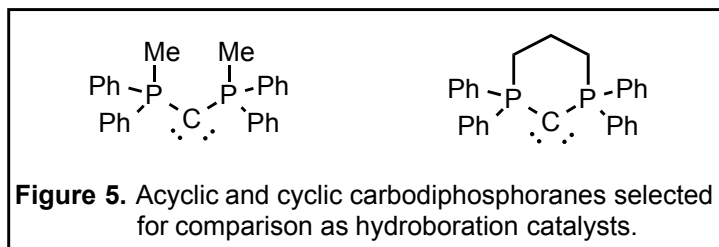
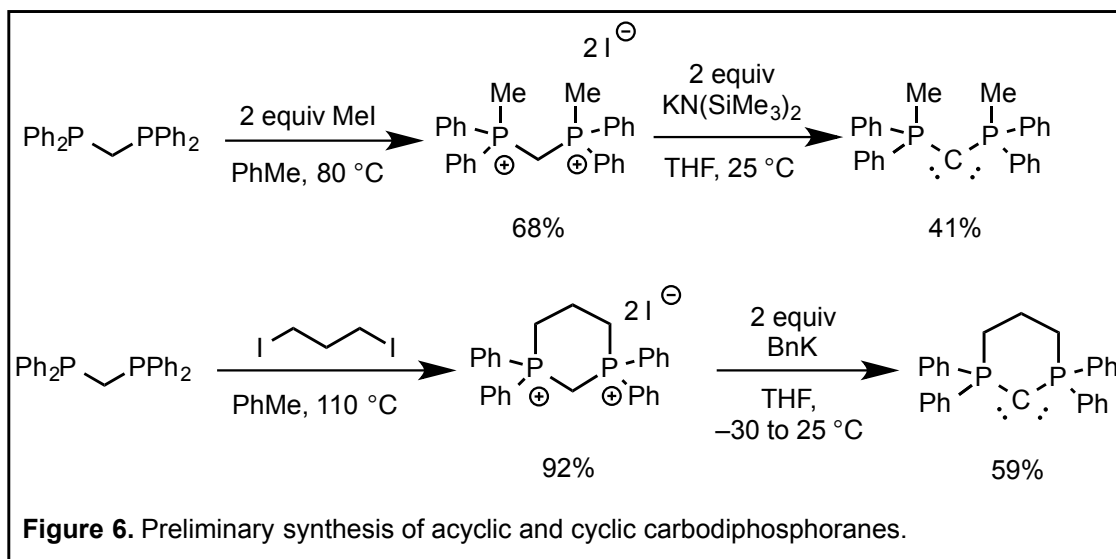


Figure 5. Although hexaphenylcarbodiphosphorane, (Ph₃P)₂C, is the most widely used carbodiphosphorane,⁴⁸ we have selected dimethyltetraphenylcarbodiphosphorane, (MePh₂P)₂C, for the proposed studies in Aims 1 and 2 because the latter is less sterically demanding, which may facilitate substrate binding during catalysis.

The acyclic (MePh₂P)₂C compound has a P–C–P angle of 122°;⁴⁹ however, this angle may be flexible, as the closely related (Ph₃P)₂C has reported P–C–P angles ranging from 130° to 180°.⁵⁰ The P–C–P angle for the phenyl-substituted six-membered ring carbodiphosphorane is 117°,⁵¹ and we anticipate the P–C–P angle should be less flexible for cyclic carbodiphosphoranes. *We hypothesize that carbodiphosphoranes with smaller P–C–P angles will be more nucleophilic, and therefore will show greater activity in hydroboration reactions.*

To date, undergraduate students in my research group (**Cara Fleener '21**, **Roxanne Naumann '21**, and **Daniel Chang '19**) have successfully synthesized both acyclic and cyclic carbodiphosphorane derivatives using our nitrogen-atmosphere glovebox (**Figure 6**). The acyclic (MePh₂P)₂C was first described by Schmidbaur and coworkers in 1976,⁵² and the reported

synthesis involves treatment of bis(diphenylphosphino)methane (dppm) with gaseous methyl bromide, followed by deprotonation using an excess of sodium amide. Undergraduate researchers in my group have successfully adapted this procedure to use methyl iodide as the alkylating reagent and two equivalents of potassium bis(trimethylsilyl)amide to perform the deprotonation step.

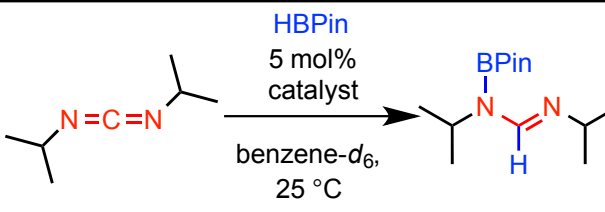


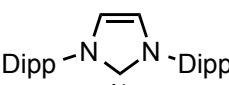
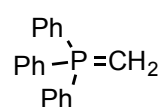
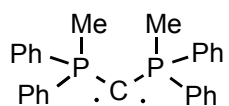
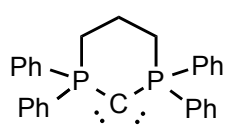
The six-membered cyclic carbodiphosporane was first reported by Schmidbaur and coworkers in 1980.⁵¹ The authors describe the synthesis as entailing double alkylation of dppm with 1,3-dibromopropane, followed by double deprotonation using methylenetriethylphosphorane, $\text{Me}_3\text{P}=\text{CH}_2$; however, detailed procedures and yields were not provided. Our group has successfully performed an adapted synthesis using 1,3-diiodopropane for the cyclization step and benzyl potassium (BnK) as the base to form the cyclic carbodiphosporane product (**Figure 6**). We have characterized both the acyclic and cyclic carbodiphosporanes by ^1H , ^{13}C , and ^{31}P NMR spectroscopy.

Aim 1.2 Optimization of Carbodiimide Hydroboration Catalysis

The two carbodiphosphoranes prepared in Aim 1.1 will be studied as catalysts for carbodiimide hydroboration. We are targeting monohydroboration of carbodiimides as a route to *N*-borylformamidine products. This transformation is rare and to our knowledge, there are no prior reports of nucleophilic catalysts for carbodiimide hydroboration. As proof-of-concept for the proposed work, we have compared a range of metal-free nucleophilic compounds as potential catalysts for carbodiimide hydroboration (**Figure 7**). Excitingly, we have observed that both the acyclic and cyclic carbodiphosphoranes described in Aim 1.1 can efficiently catalyze diisopropylcarbodiimide hydroboration at room temperature using pinacolborane (HBPin) as the reductant. In contrast, sodium tert-butoxide and the ylide $\text{Ph}_3\text{P}=\text{CH}_2$ show low hydroboration activity, while triethylphosphine oxide and an unsaturated *N*-heterocyclic carbene are inactive. These results validate the viability of carbodiphosphoranes as organocatalysts and demonstrate that the air-sensitive catalytic reactions proposed herein are within the capabilities of Chapman undergraduates.

Additional experiments will be performed to optimize hydroboration conditions for diisopropylcarbodiimide hydroboration. To investigate solvent



Catalyst	Time (h)	% conversion ^a
NaO ^t Bu	24	17%
Et ₃ PO	22	no reaction
	23	no reaction
	24	17%
	6.5	95%
	5	99%

^a Determined by ¹H NMR spectroscopy

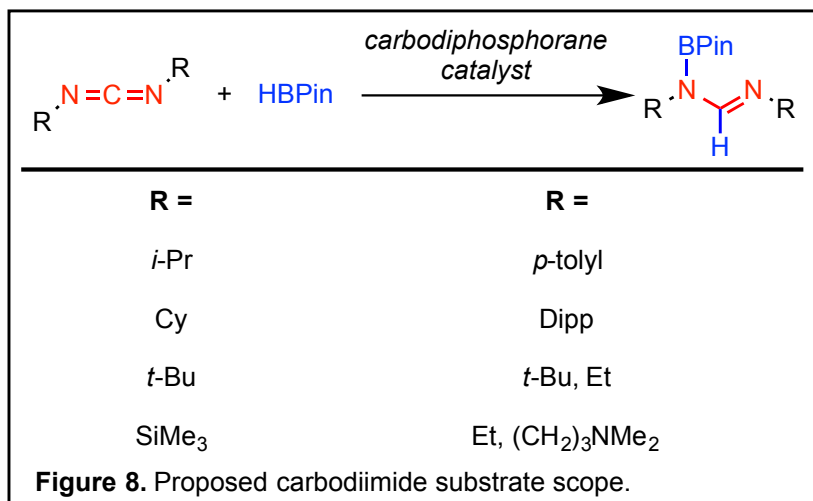
Figure 7. Preliminary comparison of nucleophilic catalysts for carbodiimide hydroboration.

effects on hydroboration rate and overall yield, catalytic reactions using the acyclic and cyclic carbodiphosphanes will be compared in benzene-*d*₆, toluene-*d*₈, dichloromethane-*d*₂, and tetrahydrofuran-*d*₈. Separately, reactions varying catalyst loading (1 mol%, 2.5 mol%, and 5 mol%) will be performed. Overall, these studies will identify reaction conditions that maximize the overall yield and achieve a reasonable rate of diisopropylcarbodiimide monohydroboration.

Aim 1.3 Carbodiimide Hydroboration Substrate Scope

Once optimal conditions for diisopropylcarbodiimide hydroboration have been identified, catalytic studies will be performed for seven additional commercially available carbodiimides (**Figure 8**). Hydroboration experiments using symmetrical substrates featuring cyclohexyl, *tert*-

butyl, and trimethylsilyl substituents will probe the influence of carbodiimide steric profile on hydroboration yield and reaction rate. Symmetrical aryl-substituted carbodiimides featuring *para*-



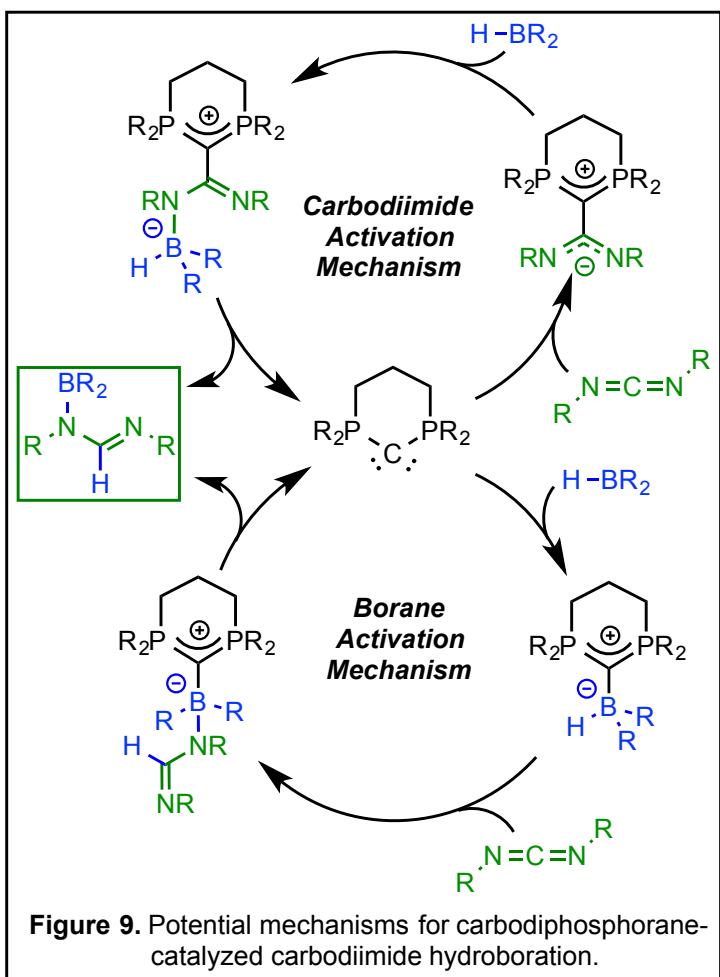
para-tolyl or 2,6-diisopropylphenyl (Dipp) substituents will also be compared. In previous hydroboration studies, aryl carbodiimides have been observed to react more slowly than alkyl carbodiimides,^{19,24} and we will determine if this trend holds for carbodiphosphorane-catalyzed reactions as well. Hydroboration of two unsymmetrically substituted alkyl carbodiimides will gauge if the installation of BPin can be accomplished regioselectively on the less sterically hindered nitrogen. The activity of the acyclic and cyclic carbodiphosphorane catalysts will be compared for all carbodiimide substrates. All catalytic reactions will be performed in J. Young

NMR tubes using deuterated solvents, and reaction conversions will be monitored by ^1H NMR spectroscopy relative to an internal standard. Hydroboration products will be characterized by ^1H , ^{11}B , and ^{13}C NMR spectroscopy, IR spectroscopy, and mass spectrometry.

Aim 1.4. Mechanistic Studies of Carbodiimide Hydroboration Catalysis

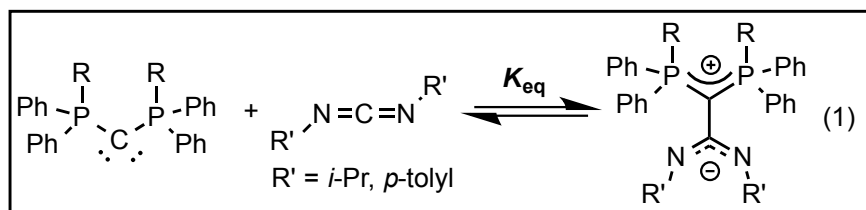
With the knowledge gained from the carbodiimide substrate scope in Aim 1.3, we will investigate the mechanism of carbodiphosphorane-catalyzed carbodiimide hydroboration. Nucleophilic organic compounds are unprecedented catalysts for these transformations, and the mechanistic insights gained through this work will be valuable for future catalyst development. Both stoichiometric and catalytic experiments will be performed to provide evidence for a plausible catalytic cycle.

We envision two potential mechanisms for carbodiimide hydroboration (labeled “Borane Activation Mechanism” and “Carbodiimide Activation Mechanism” in **Figure 9**). The nucleophilic carbodiphosphorane could coordinate to pinacolborane, rendering the borane more hydridic. Hydroboration could then occur by hydride transfer to the carbodiimide and B–N bond formation, followed by carbodiphosphorane dissociation.



Alternatively, the carbodiphosphorane could first coordinate to the carbodiimide substrate. Subsequent borane binding to the amidinate group followed by hydride transfer could furnish the *N*-borylformamidine product.

To determine reaction steps that are plausible under catalytic



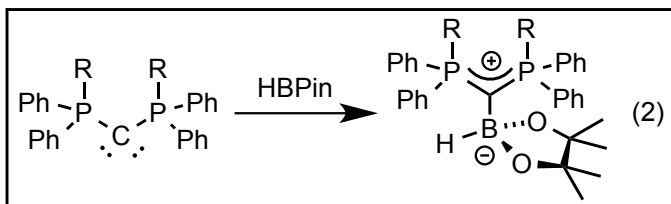
conditions, we will perform stoichiometric experiments of carbodiimides with carbodiphosphoranes. We anticipate that these reactions will result in the formation of carbodiphosphorane–carbodiimide adducts (**eq 1**). There is literature precedent for the coordination of diarylcarbodiimides to $(\text{Ph}_3\text{P})_2\text{C}$,⁵³ although the reported adducts were not fully characterized.

Equilibrium constants (K_{eq}) will be measured for isopropyl- and *p*-tolyl-carbodiimide binding to the acyclic and cyclic carbodiphosphoranes in **Figure 5**. Based on literature precedent for *N*-heterocyclic carbenes,^{54,55} we anticipate that di-*p*-tolyl-carbodiimide will have larger binding constant than diisopropylcarbodiimide. Measured K_{eq} values will be compared to hydroboration rates to determine if there is an observed trend between binding constant and hydroboration activity. Carbodiphosphorane–carbodiimide adducts will be characterized by ^1H , ^{13}C , and ^{31}P NMR spectroscopy, IR spectroscopy, elemental analysis, and X-ray crystallography.

Carbodiphosphorane–carbodiimide adducts will then be thermolyzed in an attempt to form phosphoranylideneketenimine ($\text{RPh}_2\text{P}=\text{C}=\text{C}=\text{NR}'$) species. Previous work has demonstrated that $(\text{Ph}_3\text{P})_2\text{C}$ –alkylthiocyanate adducts can be decomposed at 150 °C to form $\text{Ph}_3\text{P}=\text{C}=\text{C}=\text{NR}$ derivatives.⁵⁶ We will attempt to isolate and fully characterize phosphoranylideneketenimine derivatives formed upon the thermolysis of either acyclic and cyclic carbodiphosphoranes with

diisopropylcarbodiimide or di-*p*-tolyl-carbodiimide. Control experiments treating $RPh_2P=C=C=NR'$ products with an excess of carbodiimide and HBPIn will determine if these potential decomposition products are catalytically competent for carbodiimide hydroboration.

Separately, treatment of carbodiphosphanes with pinacolborane will be performed and monitored by 1H , ^{31}P , and ^{11}B NMR spectroscopy (eq 2). Adducts of $(Ph_3P)_2C$ with triphenylborane and BH_3 have been previously reported.^{57,58} Instead of simple adduct formation, it is possible that 1,2-



addition of the H–B bond could be observed across the central carbon and a flanking phosphorus center; this reactivity pattern has been previously observed for carbodicarbenes.⁵⁹ We will attempt to isolate and fully characterize any carbodiphosphorane–pinacolborane adducts formed.

To complement stoichiometric experiments, mechanistic studies of the catalytic hydroboration of diisopropylcarbodiimide will be performed. To determine the catalyst resting state, the reaction of carbodiphosphorane with an excess of diisopropylcarbodiimide and HBPIn will be monitored by 1H and ^{31}P NMR spectroscopy. It is possible that free carbodiphosphorane, a carbodiphosphorane–carbodiimide adduct, or a carbodiphosphorane–pinacolborane adduct could be the catalyst resting state.

Once the catalyst resting state has been probed, kinetic experiments will probe the viability of the borane activation mechanism and carbodiimide activation mechanism shown in **Figure 9**. A series of 1H NMR kinetics experiments separately varying the concentration of each reagent will analyze the dependence of the observed rate constant (k_{obs}) on the concentration of catalyst, carbodiimide, and pinacolborane. The rate law and the observed catalytic resting state will provide evidence for the hydroboration mechanism. For example, if the carbodiphosphorane–carbodiimide

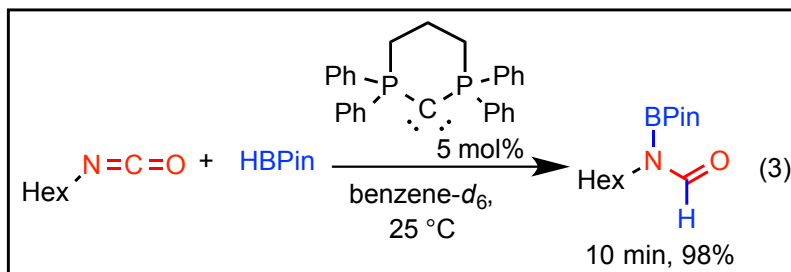
adduct is observed as the catalyst resting state, a proportional relationship between k_{obs} and [carbodiimide] would be consistent with the carbodiimide activation mechanism, whereas an inverse relationship between k_{obs} and [carbodiimide] is more consistent with the borane activation mechanism. The mechanistic insight gained in Aim 1.4 will provide fundamental understanding of catalytic pathways for carbodiphosphanes and may enable the rational design of even more active and selective nucleophilic catalysts for carbodiimide hydroboration.

Aim 2. Carbodiphosphorane-Catalyzed Isocyanate Hydroboration

Aim 2.1. Optimization of Isocyanate Hydroboration Catalysis

The second stage of our proposed research will study selective isocyanate reduction to generate formamide products. These transformations are rare, and *to our knowledge, there are no previous reports of catalytic isocyanate monohydroboration*. Excitingly, our group has observed

rapid and selective hexylisocyanate hydroboration catalyzed by a cyclic carbodiphosphorane catalyst



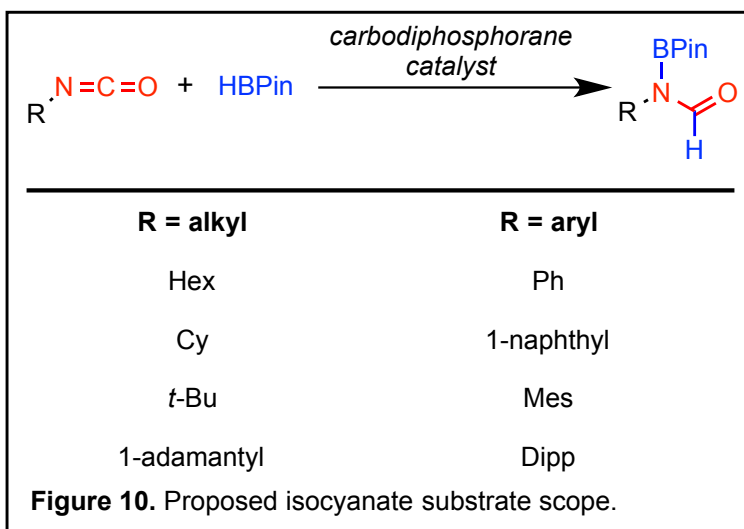
(eq 3). Complete conversion is observed by ^1H NMR spectroscopy within 10 min at room temperature using 5 mol% catalyst loading. Monohydroboration is exclusively observed, even in experiments performed using 2 equivalents of HBPin.

Additional experiments will be performed to optimize hydroboration conditions for hexylisocyanate hydroboration. We will compare the activity of acyclic and cyclic carbodiphosphanes to other classes of nucleophilic compounds such as *N*-heterocyclic carbenes and ylides. Catalytic reactions using both acyclic and cyclic carbodiphosphorane catalysts will be compared in benzene- d_6 , toluene- d_8 , dichloromethane- d_2 , and tetrahydrofuran- d_8 . Separately,

hydroboration experiments varying catalyst loading will be performed. All reactions will be monitored by ^1H and ^{11}B NMR spectroscopy, and conversion will be measured relative to an internal standard.

Aim 2.2 Isocyanate Hydroboration Substrate Scope

A series of eight commercially available isocyanates has been selected to assess hydroboration substrate scope for both acyclic and cyclic carbodiphosphorane catalysts (Figure 10). To probe the influence of alkyl steric effects on



hydroboration yield and rate, hydroboration experiments will be performed using hexyl, cyclohexyl, *tert*-butyl, and 1-adamantyl substituents. Hydroboration of four aryl isocyanates with varied steric profiles that feature phenyl, 1-naphthyl, mesityl, and 2,6-diisopropylphenyl (Dipp) substituents will be compared. Experiments will initially be attempted using 1 equivalent of pinacolborane and 5 mol% carbodiphosphorane catalyst loading at room temperature. If reactions are sluggish under these conditions, the catalyst loading or amount of HBPin reductant will be increased. All hydroborations will be performed in J. Young NMR tubes using deuterated solvents so that reactions can be conveniently monitored by ^1H and ^{11}B NMR spectroscopy. All *N*-borylformamide products will be characterized by ^1H , ^{11}B , and ^{13}C NMR spectroscopy, IR spectroscopy, and mass spectrometry. X-ray crystallography will be performed for a subset of *N*-borylformamides.

It is possible that carbodiphosphoranes may catalyze the cyclotrimerization of some isocyanates under investigation, as nucleophilic catalysts such as *N*-heterocyclic carbenes, *N*-heterocyclic olefins, and Verkade's base are known to catalyze isocyanate cyclotrimerization.^{60–62} If cyclotrimerization of some isocyanate substrates is observed using carbodiphosphorane catalysts, we will attempt hydroboration reactions using an excess of pinacolborane in an attempt to favor reduction over cyclotrimerization. If attempts to favor isocyanate hydroboration are unsuccessful, we will study the catalytic cyclotrimerization of these isocyanate substrates in the absence of HBPIn.

Aim 2.3. Mechanistic Studies of Isocyanate Hydroboration Catalysis

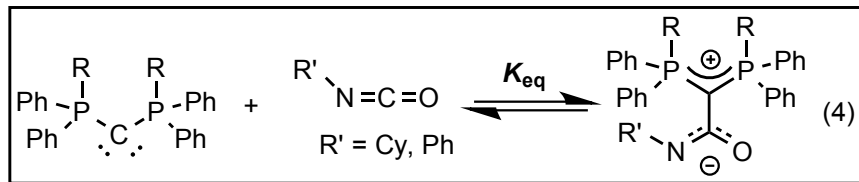
We will investigate the mechanism of carbodiphosphorane-catalyzed isocyanate hydroboration. To our knowledge, there are no reported catalysts for isocyanate monohydroboration, making the mechanistic insights gathered in Aim 2.3 valuable for future catalyst development. Both stoichiometric and catalytic experiments will be performed to provide evidence for a plausible catalytic cycle.

We envision two potential mechanisms for isocyanate hydroboration, analogous to those for carbodiimide hydroboration (**Figure 9**). The nucleophilic carbodiphosphorane catalyst could coordinate to the isocyanate substrate directly, followed by borane binding to the amidate group and hydride transfer. Alternatively, the carbodiphosphorane catalyst could coordinate to the borane substrate, followed by isocyanate insertion into the H–B bond.

Knowledge gained in Aim 1.4 for carbodiphosphorane–carbodiimide and carbodiphosphorane–borane adducts will guide our mechanistic investigations of isocyanate hydroboration. To evaluate carbodiphosphorane binding to isocyanates, stoichiometric experiments will probe the binding of cyclohexylisocyanate and phenylisocyanate to acyclic and

cyclic carbodiphosphoranes.

We anticipate that these reactions will result in the



formation of carbodiphosphorane–isocyanate adducts (**eq 4**), as there is literature precedent for the binding of $(\text{Ph}_3\text{P})_2\text{C}$ to aryl isocyanates.⁵³ All isocyanate adducts will be characterized by ^1H , ^{13}C , and ^{31}P NMR spectroscopy, IR spectroscopy, elemental analysis, and X-ray crystallography.

Carbodiphosphorane–isocyanate adducts will be heated in an attempt to observe formation of phosphoranylideneketenimine ($\text{RPh}_2\text{P}=\text{C}=\text{C}=\text{NR}'$) or phosphoranylideneketene ($\text{RPh}_2\text{P}=\text{C}=\text{C}=\text{O}$) species.⁵⁶ Control experiments treating $\text{RPh}_2\text{P}=\text{C}=\text{C}=\text{NR}'$ and $\text{RPh}_2\text{P}=\text{C}=\text{C}=\text{O}$ derivatives with an excess of isocyanate and pinacolborane will determine if these potential decomposition products are catalytically competent.

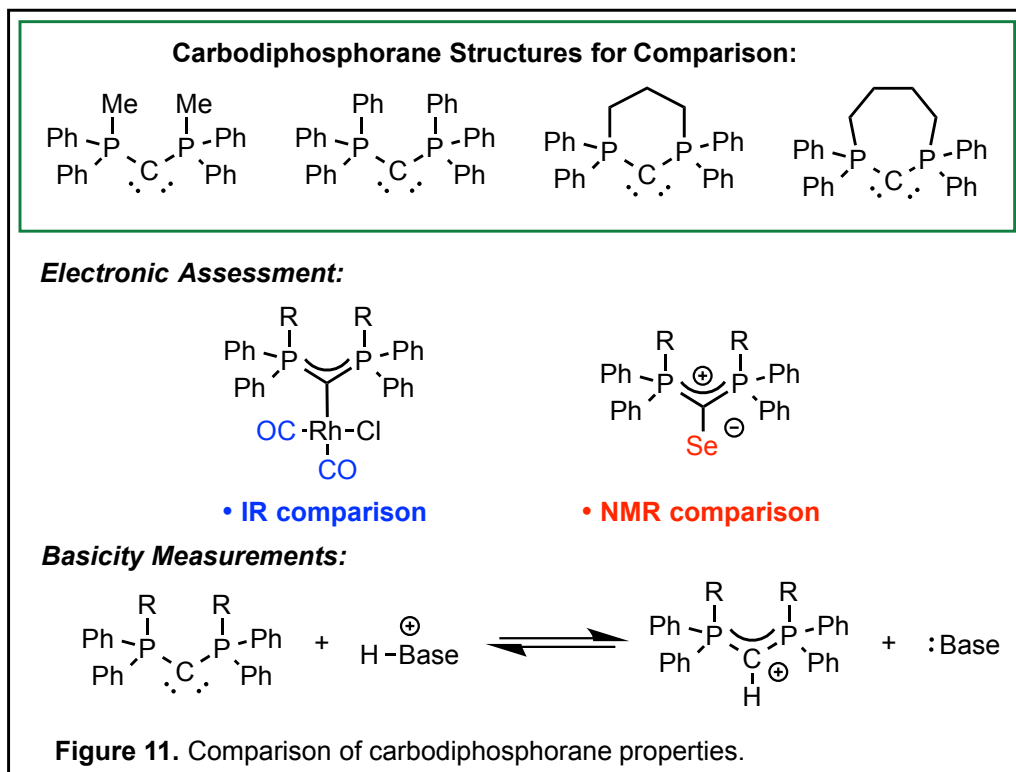
Mechanistic studies will also be performed under optimized catalytic conditions (identified in Aim 2.1). The isocyanate substrate will be chosen such that the hydroboration reaction rate is convenient for monitoring by ^1H NMR spectroscopy. To determine the catalyst resting state, the catalytic hydroboration reaction will be monitored by ^1H and ^{31}P NMR spectroscopy. ^1H NMR kinetics experiments will probe the dependence of the observed rate constant (k_{obs}) on the concentration of carbodiphosphorane catalyst, isocyanate, and pinacolborane. The mechanistic insight gained in Aim 2.3 will provide fundamental understanding of a new isocyanate monohydroboration pathway.

Aim 3: Comparison of Carbodiphosphorane Structures to Optimize Catalyst Activity

Separate from catalytic hydroboration studies, we are interested in better understanding the steric and electronic properties of carbodiphosphoranes and how these features relate to catalytic activity. To our knowledge, there are no comprehensive reports that experimentally compare steric

and electronic properties for a series of carbodiphosphoranes. This information is critical for the rational design of new carbodiphosphorane structures and the further development of carbodiphosphorane organocatalysis.

Within Aim 3, we will compare four carbodiphosphoranes, all of which have been previously reported and can be synthesized in two reaction steps (**Figure 11**).^{51,52,63} These structures have been selected to allow comparisons of (i) acyclic carbodiphosphoranes with different steric profiles, (ii) acyclic versus cyclic carbodiphosphoranes, and (iii) ring size effects for cyclic carbodiphosphoranes. Ring size is known to significantly influence the steric and electronic properties of *N*-heterocyclic carbenes;^{64–66} however, the effect of ring size on carbodiphosphorane donor or steric properties is not known.



Two spectroscopic methods will be used to compare the electronic properties of the four alkyl/aryl carbodiphosphoranes. For IR comparisons, we will prepare *cis*-

RhCl(CO)₂(carbodiphosphorane) complexes by treatment of rhodium carbonyl chloride dimer, Rh₂Cl₂(CO)₄, with two equivalents of carbodiphosphorane.⁶⁷ Solution IR spectra of rhodium complexes will be measured in dichloromethane solvent to correlate the electron-donating ability of the carbodiphosphorane ligand to the observed CO stretching frequencies of the complexes.⁶⁸ A separate NMR-based probe of electronic properties is ⁷⁷Se NMR spectroscopy of Lewis base–selenium adducts.⁶⁹ For this technique, we will prepare carbodiphosphorane–selenium adducts by treatment of free carbodiphosphoranes with selenium powder.⁷⁰ Measured ⁷⁷Se NMR chemical shifts for the carbodiphosphorane–selenium adducts will be compared as a second method to benchmark the relative donor abilities of the four selected carbodiphosphoranes.

To gain information about the steric properties of each carbodiphosphorane, RhCl(CO)₂(carbodiphosphorane) complexes will be characterized by X-ray crystallography. The percent buried volume metric of steric bulk will be calculated using the SambVca2 web tool⁷¹ with crystallographically-determined structures as a starting point.

Aims 1 and 2 examine carbodiphosphoranes as nucleophilic catalysts; however, more broadly, these compounds have the potential to serve as superbases for other organic transformations.⁷² Calculated proton affinities have been reported for several alkyl/aryl carbodiphosphoranes;⁷³ however, to our knowledge, experimental basicity measurements have not been performed for these compounds. To measure p*K*_{BH+} values for the four carbodiphosphoranes in **Figure 11**, we will perform ³¹P NMR titration experiments against phosphazene and ylide bases with known p*K*_{BH+} values in tetrahydrofuran-*d*₈.⁷⁴ We will determine if carbodiphosphorane basicities are correlated with donor properties as measured by IR and NMR spectroscopic methods.

Lastly, the carbodiimide and isocyanate hydroboration activity of the four carbodiphosphoranes from **Figure 11** will be studied by ¹H NMR spectroscopy to determine

relative reaction rates and overall hydroboration product yields for each carbodiphosphorane catalyst. These reaction comparisons are designed to determine if a relationship exists between catalytic performance and thermodynamic donor strength, percent buried volume, or basicity. Overall, these experiments offer insight into the carbodiphosphorane catalyst's electronic and steric properties, which will improve the fundamental understanding of the interplay between structure and reactivity for these organocatalysts.

Conclusion

The proposed work aims to demonstrate the synthetic utility of carbodiphosphoranes as a new class of organocatalysts. The successful completion of this proposal could result in more sustainable methods for the synthesis of nitrogen-containing molecules from readily available carbodiimide and isocyanate substrates. Furthermore, this project will serve as a foundation to develop a broad research program that investigates the synthesis and catalytic activity of carbodiphosphorane catalysts. This research will be conducted by undergraduate students, which will contribute to the education of future science professionals.

Timeline

Year 1: Optimize carbodiphosphorane-catalyzed carbodiimide catalysis (*Aim 1.2*); investigate carbodiimide substrate scope (*Aim 1.3*); initiate carbodiimide hydroboration mechanistic studies (*Aim 1.4*); optimize isocyanate hydroboration and isocyanate substrate scope (*Aims 2.1 and 2.2*).

Year 2: Complete mechanistic studies of hydroboration (*Aim 1.4*); publish results concerning carbodiimide hydroboration (*Aim 1*); perform mechanistic studies of isocyanate hydroboration (*Aim 2.3*); prepare manuscript on isocyanate hydroboration catalysis (*Aim 2*); compare electronic and steric properties of carbodiphosphoranes (*Aim 3*); present results at an ACS National Meeting.

Word Count for Proposal Narrative: 3,841 words

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