### **American Chemical Society**

#### **National Awards Nomination Packet**

ACS Award for Creative Work in Fluorine Chemistry:2018 for: Abigail Doyle

Received: 11/01/2014 Cycle Year: 3

"For the first of its kind study and broad-scale implications for the field of fluorine chemistry and for the pharmaceutical industry as a whole.

**NOMINATOR:** 

David MacMillan Tel: 626 354-7502 Fax: (609)258-6746 Princeton University Email: dmacmill@princeton.eduXXX

Director of The Merck Center Princeton, NJ 08544-0001 UNITED STATES

• Have you discussed this award nomination with the nominee?

**NOMINEE:** 

Abigail Doyle (646)645-7304 Tel:

Email: agdoyle@princeton.eduXXX Princeton University 129 Frick Laboratory

Princeton, NJ 08544-0001 UNITED STATES

ACS Current Member: Yes Years of Service:

Present Position: Associate Professor of Chemistry

Industry: Academia

**SAFETY PROTOCOLS:** 

• Does the nominee employ and require good safety protocols and practices in Yes

his/her laboratory?

• Prior Recipient? Yes

• Reason? Nominee has won at least one award in the past 5

C. Cope Early Career Scholars Award: 2014 in 20 Abby Doyle's is receiving national and international • Work Differs:

groundbreaking work in organofluorine chemistry.

No

**SUPPORTER 1** 

Amir Hoveyda Tel: (617)552-3618 (617)552-4020 Fax: **Boston College** Email: hoveyda@bc.eduXXX

2609 Beacon St Chestnut Hill, MA 02467

**UNITED STATES** 

# Princeton University Department of Chemistry Princeton, New Jersey 08544



#### David W. C. MacMillan

James S. McDonnell Distinguished University Professor of Chemistry Director, Merck Center for Catalysis at Princeton Chair, Department of Chemistry, Princeton (626) 354-7502 dmacmill@princeton.edu

October 31st, 2014

## Nomination of Professor Abigail Doyle for the ACS Award for Creative Work in Fluorine Chemistry

Please accept this letter as a nomination of Professor Abigail Doyle of Princeton University for the 2015 Award for Creative Work in Fluorine Chemistry. Along with Professor Amir Hoveyda, we provide our strongest endorsement of Abby for this prestigious award.

Research Activities. To date, Abby has launched a strong program in the area of chemical synthesis. Her research has focused on two main areas: (1) the enantioselective production of C–F stereogenicity, a critical area of research that will have broad impact on the pharmaceutical sciences and (2) the use of transition metals to catalytically access molecular entities of high value to practitioners of medicinal chemistry. In both cases, she has exercised an extremely mature level of judgment in her problem selection. It is fair to say, that she has already achieved a tremendous level of impact in both areas. With respect to her work in the area of fluorine chemistry, her reaction methodology studies have already been adopted by a range of pharmaceutical companies (Merck, Abbot to name only two).

It is well known that stereo-defined organofluorine compounds display a range of distinctive physical properties that often render them valuable to the pharmaceutical, agrochemical and polymer industries. In particular, fluorine atom incorporation has become an effective tool for medicinal chemists to tailor the physical and metabolic profiles of drug candidates. Despite the broad-spectrum utility of such C–F containing compounds, it is remarkable to consider that only a few catalytic methods exist for the asymmetric installation of fluorine onto carbogenic frameworks. The work that is coming out of Abby's lab is a direct solution to this problem. As one point of calibration, Merck Research Labs only funded two chemists on a worldwide basis during 2010. One of these grants was provided to Abby as they view her work on fluorination as both groundbreaking and of high value to the pharmaceutical sector.

As an out growth of this work Abby has extended her studies to one of the first examples of F18 chemistry that has been conducted in the area of enantioselective catalysis. This work sets the stage for the incorporation of enantiomerically pure f-containing drugs that can also be employed as PET tracers. Clearly, this first of it's kind study has broad-scale implications for the field of fluorine chemistry and for the pharmaceutical industry as a whole.

In summary, Professor Abby Doyle has built an extremely strong, cutting edge program in chemical synthesis within the Chemistry Department in Princeton. Her research group has grown from strength to strength and she is receiving national and international recognition for her groundbreaking work in organofluorine chemistry. She has proven herself to be a wonderful colleague within our department and a leader for the future. On his basis we propose that Professor Doyle is an exceptional candidate for the 2015 ACS Award for Creative Work in Fluorine Chemistry.

Sincerely yours,

David MacMillan

James S. McDonnell Distinguished University Professor of Chemistry

David Sightle

#### Abigail Gutmann Doyle

Associate Professor, Princeton University
Department of Chemistry
129 Frick Laboratory
Princeton, NJ 08544
Office phone: 609.258.1944

Cell phone: 646.645.7304 Email: agdoyle@princeton.edu

Group website: http://chemistry.princeton.edu/doylelab/

#### **EDUCATION**

2003-2008	Harvard University, Department of Chemistry and Chemical Biology Degree awarded: Ph.D., NDSEG, NSF, and Harvard Merit Pre-Doctoral Fellow Research Advisor: Professor Eric N. Jacobsen Doctoral Thesis: Engaging Alkyl Halides and Oxocarbenium Ions in Asymmetric Catalysis.
2002-2003	Stanford University, Department of Chemistry NDSEG Pre-Doctoral Fellow Research Advisor: Professor Justin Du Bois Studies Directed Towards the Hydration of Unactivated Alkenes Catalyzed by Gold Complexes.
1998-2002	Harvard University, Department of Chemistry and Chemical Biology Degree awarded: A.B. and A.M. with Highest Honors, summa cum laude Research Advisor (2000-2002): Professor Eric N. Jacobsen Development of a Synthetically Useful MMO Mimic System for Alkene Epoxidation.

#### PROFESSIONAL AND ACADEMIC EXPERIENCE

#### Associate Professor of Chemistry, Princeton University (July 2013 to present)

- In collaboration with the MacMillan group (Princeton), identified a new cross-coupling paradigm in which the combination of photoredox catalysis and nickel catalysis enables C(sp3)–C bond formation from simple and readily available organic molecules. We described decarboxylative and C–H functionalization of carboxylic acids and anilines with aryl halides to generate valuable amine and ether products.
- Demonstrated the first enantioselective incorporation of <sup>18</sup>F into an organic substrate; this process uses the immediate source of <sup>18</sup>F obtained from the cyclotron in a mild, rapid, and operationally convenient procedure. The process enables enantioselective access to experimental and clinically-validated radiotracers by late-stage radiofluorination.
- Identified a novel ligand class that imparts unique electronic properties to a transition metal catalyst compared with state-of-the-art ligands for cross-coupling catalysis. As such, these ligands promote valuable reactions previously not possible using phosphines, amines, and N-heterocyclic carbenes. This ligand class is straightforward to prepare from inexpensive and commercial components and can be tuned to influence reaction rates and selectivity. We have also prepared chiral variants of the ligand class and shown that these serve as novel chiral ligands for asymmetric catalysis.

#### Assistant Professor of Chemistry, Princeton University (July 2008 to June 2013)

- Mentored 4 postdoctoral fellows, 12 graduate students, and 8 undergraduate researchers.
- Discovered the first asymmetric catalytic methods for nucleophilic fluorination, including cooperative catalytic
  systems for asymmetric ring opening of epoxides and aziridines, and two Pd-catalyzed protocols for enantioand regioselective allylic fluorination.

- Conducted in depth mechanistic studies of these methods using physical organic, organometallic, and computational techniques that have uncovered fundamental insights in the areas of cooperative catalysis and transition metal-catalyzed fluorination.
- Identified catalytic cross-coupling reactions with styrenyl epoxides and aziridines as electrophiles. The
  methodologies feature unique ligand effects for nickel catalysis that enable regioselective C<sub>sp</sub>3–O and C<sub>sp</sub>3–N
  activation and mild C<sub>alkyl</sub>–C bond formation.
- Discovered a dual-activation strategy that permits the acid- and base-free synthesis of amines and ethers by Suzuki cross coupling with allylic N,O- and O,O-acetals.
- Elucidated a new entry to alkyl cross coupling that involves oxidative interaction of a nickel catalyst with iminium and oxocarbenium electrophiles; this approach has led to the identification of enantioselective methods for the preparation of important chiral heterocyclic products.

#### Graduate Research Assistant, Harvard University (September 2003 to June 2008, Jacobsen laboratory)

- National Defense Science and Engineering, National Science Foundation, and Harvard Merit Pre-Doctoral Fellow
- Sigma-Aldrich Graduate Student Innovation Award and Christensen Prize for Outstanding Research Achievement
- Identified asymmetric catalytic methods for the alkylation of enolates that afford access to cyclic and acyclic ketones bearing α-quaternary all-carbon stereogenic centers.
- Worked in collaboration with post-doctoral fellow Dr. Sarah Reisman to discover a novel approach for the enantioselective addition of nucleophiles to oxocarbenium ions promoted by a thiourea catalyst.
- Co-authored a *Chemical Review* article on hydrogen-bond donor catalysis that has received >720 citations.

#### Teaching Assistant, Harvard University (Fall 2003 & 2006)

- Graduate level Organometallic Chemistry
- First-semester undergraduate organic chemistry for non-majors, Head Teaching Fellow
- Harvard College Certificate of Distinction in Teaching

#### Graduate Research Assistant, Stanford University (August 2002 to July 2003, Du Bois laboratory)

- National Defense Science and Engineering Fellow
- Performed organometallic research on the preparation of Au(III) complexes and evaluation of their reactivity for the hydration of unactivated alkenes.
- Cumulative GPA: 4.0

#### Teaching Assistant, Stanford University (Spring 2003)

• Second-semester undergraduate organic chemistry.

#### Undergraduate Teaching Assistant, Harvard University (Spring 2002)

• Undergraduate organic chemistry.

#### Undergraduate Research Assistant, Harvard University (September 2000 to June 2002)

- Pfizer Summer Undergraduate Research Fellow
- Worked with post-doctoral fellow Dr. M. Christina White to elucidate the scope and mechanism of a novel iron-catalyzed epoxidation reaction of terminal alkenes and to design chiral ligands for an asymmetric variant of the reaction.

#### Summer Intern, Bristol-Myers Squibb, Discovery Chemistry (Metabolic Diseases, May to August 2000)

• Elucidated the scope of a new reaction for the selective reduction of anomeric ketals in the synthesis of C-arylglucosides; this reaction has been used to prepare the type II diabetes treatment Dapagliflozin.

#### **AWARDS & HONORS**

- Phi Lambda Upsilon National Fresenius Award (2014)
- Presidential Early Career Award for Scientists and Engineers (2012)
- Novartis Chemistry Lectureship (2014/2015)
- Bayer Excellence in Science Award (2013)
- Arthur C. Cope Scholar Award (2013)
- Camille-Dreyfus Teacher Scholar Award (2013)
- Thieme Chemistry Journals Award (2013)
- Amgen Young Investigator Award (2012)
- Alfred P. Sloan Foundation Fellowship (2012)
- NSF CAREER Award (2012-2017)
- Roche Early Excellence in Chemistry Award (2012)
- Eli Lilly Grantee Award (2012-2014)
- Boehringer Ingelheim New Investigator Award (2012)
- Merck Award for Selective Fluorination (2010-2012)
- ACS PRF Doctoral New Investigator Grant (2009)
- Sanofi Aventis New Faculty Award (2008)
- Eli Lilly New Faculty Award (2008)
- Harvard Merit Fellowship (2007)
- Sigma-Aldrich Graduate Student Innovation Award (2006)
- Christensen Prize for Outstanding Research Achievement (2005)
- National Science Foundation Pre-Doctoral Fellowship (2004-2007)
- National Defense Science and Engineering Pre-Doctoral Fellowship (2002-2004)
- Harvard College Certificate of Distinction in Teaching (2004)
- Phi Beta Kappa Junior Inductee (2001)
- Pfizer Undergraduate Summer Research Fellowship (2001)
- Harvard College Research Fellowship Award (2001)
- Harvard Detur Prize Recipient (1999)

#### PRESENTATIONS & INVITED LECTURES

85 invited lectures since 2008

#### **PROFESSIONAL ACTIVITIES**

#### Outside Service

- Early career reviewer, SBCA, NIGMS (2012)
- Grant reviewer for National Science Foundation (2012-present)
- Grant reviewer for American Chemical Society Petroleum Research Fund (2009-present)
- Consultant at Merck (2011-present)
- Co-organizer of the 42<sup>nd</sup> National Organic Chemistry Symposium (2010-2011)
- Session chair for ACS National Meeting (Boston, MA) & Gordon Research Conferences (2009-present)
- Organized and performed chemistry demonstrations for children at Trenton Science Museum's Super Science Saturday (2011-present)
- Faculty mentor for Mercer County Community College honors chemistry program (2011-present)
- Outside reader and examiner for graduate students in the Chemistry Department at Columbia University
- Reviewer for ACS, Wiley, Elsevier, Nature Publishing Group, and Royal Society of Chemistry journals;

reviewed over 100 manuscripts since 2008

• Member of the American Chemical Society (2002-present)

#### Princeton University Service

- Member, Women in STEM Working Group at Princeton (2014-present)
- Member, Staffing and Long Range Planning Committee in Princeton Chemistry (2013-present)
- Member, Princeton Chemistry Diversity Committee (2013–present)
- Member, Princeton Chemistry Academic Review Committee (2013–present)
- Member, Committee of Committees (2013-2015)
- Chair of the Organic Chemistry Seminar Series (2008-present)
- Chair of the Organic Graduate Admissions Committee (2008-present)
- Member of the Graduate Work Committee (2008-present)
- Member of the Junior Faculty Search Committee (2008-2011)
- Member of the Instrumentation Committee (2010-present)
- Created new graduate course "Chem 536," which has been offered as part of Princeton University's Industrial Affiliates Program (2009-present)
- Initiated new Student Invited Lecture Series (SILS) in collaboration with the Chemistry Graduate Student Organization (2009-present)
- Grader for incoming Chemistry graduate student's organic placement exam (2008-2011)
- Second reader for 12 graduate dissertations (2009-present)
- Committee member for the Final Public Oral and Independent Proposal of 23 students (2008-present)
- General exams committee member for 33 students (8 of my own, 16 as advisory committee member, and 9 as assigned chair) (2008-present)
- Presented the organic research overview at Princeton's graduate student recruiting weekends (2008–2011)
- Delivered "Introduction to Research" seminar in Junior Undergraduate Colloquia series and to first-year Chemistry graduate students (2008-present)
- Faculty panel member for Princeton's incoming women in science, engineering, and mathematics (2009-present)
- Roundtable discussion facilitator for Princeton's undergraduate chemistry club dinner series (2011-present)
- Grader for undergraduate organic prize exams (2010-present)
- Reader and external grader for organic undergraduate senior theses (2010-present)
- Mentored 11 juniors for their junior paper exercise (2008-present)

#### **ACTIVE COLLABORATORS**

- Professor Per-Ola Norrby (Department of Chemistry, University of Gothenburg)
- Professors Hank Kung and Robert Mach (Department of Radiology, University of Pennsylvania)
- Drs. Shane Krska and Matthew Tudge (Automated Synthesis and Catalysis, Merck Research Laboratories)
- Drs. Sam Bonacorsi and David Donnelly (Imaging, Bristol-Myers Squibb)

#### **TEACHING EXPERIENCE**

Spring 2014	Chemistry 532: Mechanistic and Physical Organic Chemistry (graduate-level): Co-Instructor Average Rating 4.3/5.0 for Overall Quality of Course
Fall 2011, 2012	Chemistry 303: Organic Chemistry I (undergraduate-level): Co-Instructor Average Rating 3.5/5.0 for Quality of Lectures (enrollment: 300)
Spring 2009–2013	Chemistry 536: Methods for Complex Organic Synthesis (upper-level): Instructor

Average Rating 4.9/5.0 for Quality of Lectures

Fall 2009, 2010, 2014 Chemistry 530: Synthetic Organic Chemistry (graduate-level): Co-Instructor

Average Rating 4.7/5.0 for Quality of Lectures

Fall 2006 Chemistry 17: Principles of Organic Chemistry (undergraduate-level): Head Teaching Fellow

Fall 2004 Chemistry 253: Organotransition Metal Chemistry (graduate-level): Teaching Fellow

Fall 2003 Chemistry 35: Organic Monofunctional Compounds (undergraduate-level): Teaching Assistant

Spring 2002 Chemistry 20: Organic Chemistry (undergraduate-level): Teaching Fellow

#### **OUTREACH ACTIVITIES**

Trenton Science Museum, Super Science Saturday (Spring 2011–2013)

- Faculty mentor for Mercer Country Community College Honors Chemistry Program (2012)
- Faculty panel member for Princeton's incoming women in science, engineering, and mathematics (2009-present)
- Roundtable discussion facilitator for Princeton's undergraduate chemistry club dinner series (2011-present)

#### Abigail Gutmann Doyle

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DOB: April 30, 1980; Princeton, NJ Email: agdoyle@princeton.edu

Group website: http://chemistry.princeton.edu/doylelab/

#### PUBLICATIONS (INDEPENDENT RESEARCH CONTRIBUTIONS)

**27.** Zuo, Z.; Ahneman, D.; Chu, L.; Terrett, J.; Doyle, A. G.; MacMillan, D. W. C. Merging photoredox with nickel catalysis: **Coupling of α-carboxyl sp3-carbons with aryl halides**. *Science* **2014**, *345*, 437–440.

Highlighted in: \* Halford, B. A Marriage of Catalysts C&ENews 2014, 92, 9.

\* Lloyd-Jones, G. C.; Ball, L. T. **Self-control tames the coupling of reactive radicals.** *Science* **2014**, *345*, 381.

- 26. Huang, C.-Y. (Dennis); Doyle, A. G. The Chemistry of Transition Metals with Three-Membered Ring Heterocycles. *Chem. Rev.* 2014, *114*, 8153–8198.
- 25. Graham, T. J. A.; Lambert, R. F.; Ploessl, K.; Kung, H. F.; Doyle, A. G. Enantioselective radiosynthesis of positron emission tomography (PET) tracers containing [18F] fluorohydrins. J. Am. Chem. Soc. 2014, 136, 5291–5294.

Highlighted in: \* Liang, S. H.; Vasdev, N. C(sp³)–18F Bond Formation by Transition-Metal-Based

[18F] Fluorination. Angew. Chem. Int. Ed. 2014 DOI:10.1002/anie.201407065

\* Synfacts **2014**, 10, 717.

\* Halford, B. PET Project C&ENews 2014, 92, 33.

24. Katcher, M. H.; Norrby, P.-O.; Doyle, A. G. Mechanistic Investigations of Palladium-Catalyzed Allylic Fluorination. *Organometallics*. 2014, *33*, 2121–2133.

Highlighted in: \* Selected as ACS Editors' choice article and as cover issue.

- \* Top most downloaded article in Organometallics between January-May 2014
- 23. Shields, J. D.; Ahneman, D. T.; Graham, T. J. A.; Doyle, A. G. Enantioselective, Nickel-Catalyzed Suzuki Cross-Coupling of Quinolinium Ions. *Org. Lett.* 2013, *16*, 142–145.
- 22. Nielsen, D. K.; Huang, C.-Y. (Dennis); Doyle, A. G. Directed Nickel-Catalyzed Negishi Cross Coupling of Alkyl Aziridines. J. Am. Chem. Soc. 2013, 135, 13605–13609.
- 21. Braun, M.-G.; Doyle, A. G. Palladium-Catalyzed Allylic C-H Fluorination. J. Am. Chem. Soc. 2013, 135, 12990–12993.

Highlighted in: \* Ritter, S. K. Olefins Easily Flagged with Fluorine. C&ENews 2013, 91, 42.

- \* Top most downloaded article in *IACS* in August & September
- 20. Chau, S. T.; Lutz, J. P.; Wu, K.; Doyle, A. G. Nickel-Catalyzed Enantioselective Arylation of Pyridinium Ions: Harnessing an Iminium Ion Activation Mode. *Angew. Chem., Int. Ed.* 2013, *52*, 9153–9156.

Highlighted in: \* Synfacts 2013, 9, 1198.

19. Kalow, J. A.; Doyle, A. G. Enantioselective fluoride ring opening of aziridines enabled by cooperative Lewis acid catalysis. *Tetrahedron*, 2013, 69, 5702–5709.

\* Part of a Symposium-in-Print issue in honor of Prof. Melanie Sanford winning the Tetrahedron Young Investigator Award.

Highlighted in: \* Synfacts 2013, 9, 967.

18. Braun, M.-G.; Katcher, M. H.; Doyle, A. G. Carbofluorination via a Palladium-Catalyzed Cascade Reaction. Chemical Science, 2013, 4, 1216–1220.

Highlighted in: \* Top ten most downloaded articles for January–March 2013.

- 17. Sylvester, K. T.; Wu, K.; Doyle, A. G. Mechanistic Investigations of the Nickel-Catalyzed Suzuki Reaction of N,O-Acetals: Evidence for Boronic Acid-Assisted Oxidative Addition and an Iminium Activation Pathway. J. Am. Chem. Soc. 2012, 134, 16967–16970.
- 16. Kalow, J. A.; Schmitt, D. E.\*; Doyle, A. G. Synthesis of β-Fluoroamines by Lewis Base-Catalyzed Hydrofluorination of Aziridines. *J. Org. Chem.* 2012, 77, 4177–4183.

Highlighted in: \* Top ten most downloaded articles for April and May 2012

\* Undergraduate co-author

15. Huang, C.-Y. (Dennis); Doyle, A. G. Nickel-Catalyzed Negishi Alkylations of Styrenyl Aziridines. J. Am. Chem. Soc. 2012, 134, 9541–9544.

Highlighted in: \*Top ten most downloaded articles for March and April 2012

\* Selected by the JACS editors for the cover issue and as a Spotlight article (DOI: 10.1021/ja3050647)

\* Synfacts 2012, 8, 1018

14. Graham, T. J. A.; Doyle, A. G. Nickel-Catalyzed Cross Coupling of Chromene Acetals and Boronic Acids. Org. Lett. 2012, 14, 1616–1619.

Highlighted in: \*Top ten most downloaded articles for February 2012

\* McLaughlin, M.; Widegren, M.; Paul, S.; Ramirez, A.; Richardson, P.; Zlota, A.; Laird, T. Some Items of Interest to Process R&D Chemists and Engineers. *Org. Proc. Res. Dev.* **2012**, *16*, 716–726.

13. Katcher, M. H.; Sha, A.; Doyle, A. G. Regio- and Enantioselective Fluorination of Acyclic Allylic Halides. J. Am. Chem. Soc. 2011, 133, 15902–15905.

Highlighted in: \*Top ten most downloaded articles for September 2011

\* Palladium-Catalyzed Enantioselective Fluorination of Allylic Halides. Synfacts 2011, 1316.

12. Kalow, J. A.; Doyle, A. G. Mechanistic Investigations of Cooperative Catalysis in the Enantioselective Fluorination of Epoxides. J. Am. Chem. Soc. 2011, 133, 16001–16012.

Highlighted in: \*Enantioselective Fluorination of Epoxides via Cooperative Catalysis. Synfacts 2011, 1317.

11. Nielsen, D. K.; Doyle, A. G. Nickel-Catalyzed Cross Coupling of Styrenyl Epoxides with Boronic Acids.

Angew. Chem., Int. Ed. 2011, 50, 6056–6059.

- \* McLaughlin, M.; Zhao, W.; Zlota, A.; Laird, T. Some Items of Interest to Process R&D Chemists and Engineers. Org. Proc. Res. Dev. 2011, 15, 1216–1221.
  - \* Nickel-Catalyzed Opening of Styrenyl Epoxides with Boronic Acids. Synfacts 2011, 996.
- 10. Graham, T. J. A.; Doyle, A. G. Transition Metal-Catalyzed Cross Coupling with N-Acyliminium Ions Derived from Quinolines and Isoquinolines. *Chem. Sci.* 2011, 2, 980–984.
  - Highlighted in: \*Top ten most downloaded articles for February, March, April, and May 2011
- 9. Shaw, T. W.; Kalow, J. A.; Doyle, A. G. Fluoride ring-opening kinetic resolution of terminal epoxides: preparation of (S)-2-fluoro-1-phenylethanol. Org. Syn. 2012, 89, 9–18.
  - Highlighted in: \* Selected by the Editorial Board as the "Featured Article" on the Organic Syntheses homepage
- 8. Katcher, M. H.; Doyle, A. G. Palladium-Catalyzed Asymmetric Synthesis of Allylic Fluorides. J. Am. Chem. Soc. 2010, 132, 17402–17404.
  - \* McLaughlin, M.; Wilson, I.; Delaney, P.; Zhao, W.; Zlota, A.; Laird, T. Some Items of Interest to Process R&D Chemists and Engineers. Org. Proc. Res. Dev. 2011, 15, 306–313.

    \*Top ten most downloaded articles for 12 months following publication in JACS
- 7. Kalow, J. A.; Doyle, A. G. Enantioselective Ring-Opening of Epoxides by Fluoride Anion Promoted by a Cooperative Dual Catalyst System. *J. Am. Chem. Soc.* 2010, *132*, 3268–3269.
  - \* McLaughlin, M.; Garcia Rubio, S.; Wilson, I.; Zhao, W.; Laird, T.; Zlota, A. Some Items of Interest to Process R&D Chemists and Engineers. Org. Proc. Res. Dev. 2010, 14, 750–758.
    - \* Asymmetric Synthesis of Fluorohydrins. Synfacts 2010, 673.
    - \* Enantioselective Ring Opening of Epoxides by Fluoride Anion. Synform 2010, A58.
    - \*Top ten most downloaded articles for February, March, and April 2010

#### PUBLICATIONS (GRADUATE & UNDERGRADUATE RESEARCH CONTRIBUTIONS)

- 6. Reisman, S. E.; Doyle, A. G.; Jacobsen, E. N. Enantioselective Thiourea-Catalyzed Additions to Oxocarbenium Ions. J. Am. Chem. Soc. 2008, 130, 7198–7199.
- 5. Doyle, A. G.; Jacobsen, E. N. Small-Molecule H-Bond Donors in Asymmetric Catalysis. *Chem. Rev.* 2007, 107, 5713–5743.
- 4. Doyle, A. G.; Jacobsen, E. N. Enantioselective Alkylation of Acyclic α,α-Disubstituted Tributyltin Enolates Catalyzed by a Cr(salen) Complex. Angew. Chem., Int. Ed. 2007, 46, 3701–3705.
- 3. Doyle, A. G.; Jacobsen, E. N. Enantioselective Alkylations of Tributyltin Enolates Catalyzed by Cr(salen)Cl: Access to Enantiomerically Enriched All-Carbon Quaternary Centers. J. Am. Chem. Soc. 2005, 127, 62-63.
- 2. Ellsworth, B. A.; Doyle, A. G.; Patel, M.; Caceres-Cortes, J.; Meng, W.; Deshpande, P. P.; Pullockaran, A.; Washburn, W. N. C-Arylglucoside synthesis: triisopropylsilane as a selective reagent for the reduction of an anomeric C-phenyl ketal. *Tetrahedron-Asymmetry* 2003, 14, 3243–3247.

1.	White, M. C.; Doyle, A. G.; Jacobsen, E. N. A Synthetically Useful, Self-Assembling MMO Mimic System for Catalytic Alkene Epoxidation with Aqueous H <sub>2</sub> O <sub>2</sub> . J. Am. Chem. Soc. 2001, 123, 7194–7195.		



Amir H. Hoveyda Patricia and Joseph T. '49 Vanderslice Millennium Professor & Chairperson of Chemistry October 25, 2014

Dear Colleagues:

It gives me great pleasure to nominate **Professor Abigail G. Doyle** to receive the American Chemical Society Award for *Creativity in Fluorine Chemistry*.

In her six years as a faculty member at Princeton, Doyle has established an original, vibrant, productive, and impactful research program that is focused on invention of new approaches to catalysis and chemical synthesis. Her group's efforts have culminated in the identification of broad scope strategies that substantially improve the way a chemist can prepare a variety of molecules of interest whether it is in the context of a natural product total synthesis, to access a medicinally active agent, or organic materials that might possess specific beneficial attributes. What distinguishes Doyle's approach from those of his peer and the large majority of the more senior investigators in her field are the depth and rigor of her analysis and the desire to go the necessary distance in order to obtain a detailed and fundamental understanding of chemical reactivity and/or selectivity. As an independent investigator, Doyle has published 21 peer-reviewed papers in high-profile journals. These manuscripts have been the focus of "Highlight" articles in exacting scientific journals such as *Science* and *JACS*. Abby's extraordinary achievements have been recognized widely, notably in the form of a *National Fresenius Award*, a *Presidential Early Career Award*, an *American Chemical Society Arthur C. Cope Scholar Award*, a *Camille-Dreyfus Teacher Scholar Award* as well as an *Alfred P. Sloan Foundation Fellowship*.

A central feature of Doyle's activities is to design and develop new, efficient and stereoselective catalytic methods for C–F bond formation. She has been able to conceive a daring program in an area that is of interest to many laboratories, some significantly larger than hers, across the country and the world. And yet, Abby Doyle, through her marked creativity, intelligence and perseverance, has brilliantly succeeded in generating a number of remarkably effective and selective C–F bond forming approaches that are mechanistically intriguing as well. Specifically,

Doyle has introduced two noteworthy strategies for catalytic C–F bond generation. I briefly summarize these approaches below.

One of Doyle's strategies involves (salen)Co-catalyzed opening of *meso* epoxides, which can be used to access a wide variety of cyclic and acyclic F-containing molecules of exceptional enantiomeric purity (*JACS* **2010**, 3268). This is clearly a useful method, but what clearly shows this is a deep thinking young scholar, is the beautifully detailed report regarding her mechanistic investigations that resulted in her team being able to not only understand the intricacies of the catalytic process, which then allowed her to improve substantially the rate and selectivity of the transformation (*JACS* **2011**, 16001). It is impressive that through such studies, she has successfully identified that an appropriate amine co-catalyst would be desirable. Research in catalysis and reaction development does not get better than this. Much of the aforementioned chemistry has enjoyed rapid adoption by practitioners of medicinal and process chemistry, and the numerous follow-up studies from independent academic laboratories highlights its significant impact on the field. What's more, Doyle and her team have successfully shouldered the challenge of developing an enabling (fast, mild, and operationally robust) late-stage radio-fluorination protocol for <sup>18</sup>F PET. Such an achievement underscores the breadth and fearlessness of Doyle's approach.

On a second notable front, Doyle's investigations on centered on allylic substitution reactions that are catalyzed by phosphine—Pd complexes and convert allylic halides — substrates that are trivial to access — to prized allylic fluorides (*JACS* **2010**, 17402 and *JACS* **2011**, 15902). I am intimately familiar with area of catalytic enantioselective allylic substitutions, and I know well how useful and effective this approach can be; this is clearly another grand slam by the Doyle and her research team. These are reactions that furnish enantiomerically enriched allylic fluorides that cannot be prepared easily by any other protocol and can be readily functionalized in so many ways. For example, catalytic cross-metathesis would yield a gamut of other F-containing unsaturated molecules primed for a large assortment of manipulations.

Doyle's program has made several meaningful contributions to the area of fluorine research, each creative and highly impactful, which have and will continue to germinate additional activities in the critical area of catalytic stereoselective C–F bond forming processes. This remarkable young woman scholar has done so much in such short amount of time; she is truly deserving of this important honor.

Sincerely,

4-4-