

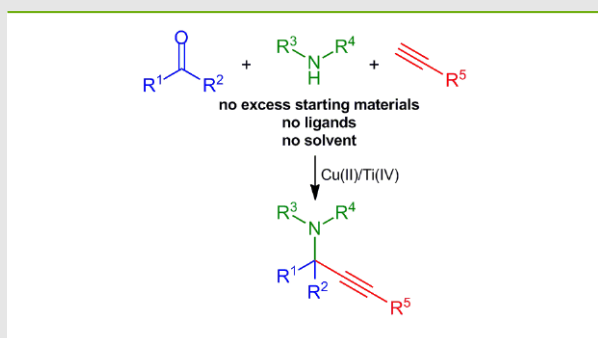
SYNFORM

People, Trends and Views in Synthetic Organic Chemistry

2013/04

SYNSTORIES ■ ■ ■ ■

■ **Copper/Titanium Catalysis Forms Fully Substituted Carbon Centers from the Direct Coupling of Acyclic Ketones, Amines, and Alkynes**



■ **Phosphine-Based Redox Catalysis in the Direct Traceless Staudinger Ligation of Carboxylic Acids and Azides**

■ **Regioselective Synthesis of Multi-substituted Furans via Metallo-radical Cyclization of Alkynes with α -Diazocarbonyls: Construction of Functionalized α -Oligofurans**

■ **Young Career Focus: Professor Jimmy Wu (Dartmouth College, Hanover, NH, USA)**

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Your opinion about SYNFORM is welcome, please correspond if you like:
marketing@thieme-chemistry.com



Thieme



Dear readers,

Is it just me, or are weekends actually tougher than the normal Monday to Friday working week? I don't know you, but most of my weekends are simply exhausting. It typically starts with a rush to the supermarket for the weekly shopping, then there is my son's first football match, the one with the school's team. It's something I really enjoy, so I never miss it. Then I prepare the lunch while my wife takes care of the little footballer's shower and my daughter obviously does nothing to help... Then, there is either the house cleaning or, if I am under pressure with my academic job, I will escape to my office. Then, I'll prepare the dinner, load the dish-washer and finally, on an ideal Saturday night, I'll collapse on the couch to watch a well-deserved TV movie with my favorite single malt. On Sunday, it's even tougher. It starts early with my son's second football match, this time with his official team, which often involves a short journey to a neighboring village. Then back home for lunch, tidying up, then Sunday afternoon is usually **SYNFORM's** time (which I really enjoy). When I am done, I take care of the dinner (Italians don't like take-away food, not even when they are in Scotland, they always cook...), final tidying-up of dining room and kitchen, and finally... well this is actually a secret. Do you know what happens on Sunday night? I check the scores of my Fantasy Football Team! Oh yes! It's a lot of fun, and I really enjoy playing against my old Italian colleagues and friends. Finally, it's bed time. It's almost Monday, at last!

Now, more seriously, let's have a look at this new issue of **SYNFORM**. We start with a new quaternary-carbon forming process developed by Professor C. H. Larsen (USA). We continue with a very convenient novel Staudinger-type amide-bond formation reported by Professor B. Ashfeld (USA). The third **SYNSTORY** covers the regioselective synthesis of highly functionalized furans discovered by Professor P. Zhang (USA). The issue is completed by a Young Career Focus on Prof. J. Wu (USA).

By the way, luckily not all of my weekends are like the one described above...

Enjoy your reading!

Matteo Zanda

Editor of **SYNFORM**

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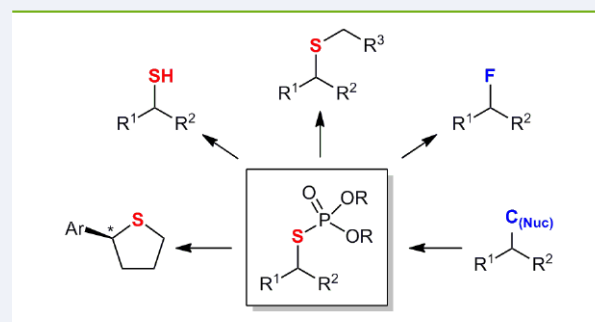
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CONTACT +++++

If you have any questions or wish to send feedback, please write to Matteo Zanda at:
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NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■

Copper/Titanium Catalysis Forms Fully Substituted Carbon Centers from the Direct Coupling of Acyclic Ketones, Amines, and Alkynes

Angew. Chem. Int. Ed. **2012**, *51*, 12289–12292

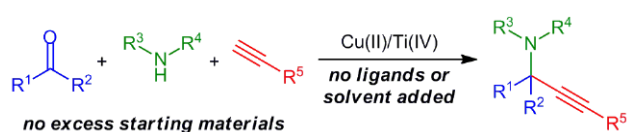
■ Three-component couplings (3CC) of aldehydes, amines and nucleophiles are ubiquitous and extremely versatile; however, the use of ketones is notoriously challenging.¹ In 2007, Prakash and Olah unveiled that gallium(III) triflate catalyzed the first direct 3CC Strecker reaction of ketones in the *Proceedings of the National Academy of Sciences*.² Terminal alkynes as nucleophiles provide propargylamines, which display an impressive range of therapeutic activity from achiral hypertensives¹ to chiral HIV reverse transcriptase inhibitors.³ Similarly, amines on fully substituted carbon centers are found in many natural products and bioactive compounds.⁴ However, ketones could not be utilized as electrophiles in these 3CC because of the high barrier to in situ ketimine formation as compared to spontaneous condensation to aldimine. Stoichiometric metal-acetylide additions to isolated ketimine represented the prior route to these compounds.³ The recent communication from the research group of Professor Catharine Larsen from the University of California, Riverside (USA) (covered in this **SYNSTORY**) bridges the synergistic chemical potential of amines and acyclic ketones by providing an efficient catalytic route to synthesize propargylamines bearing fully substituted carbon centers directly from unactivated ketones. Professor Larsen said: “The value of our method is derived from the difficulty presented by the corresponding 3CC of an acyclic ketone, an amine and a nucleophile.”

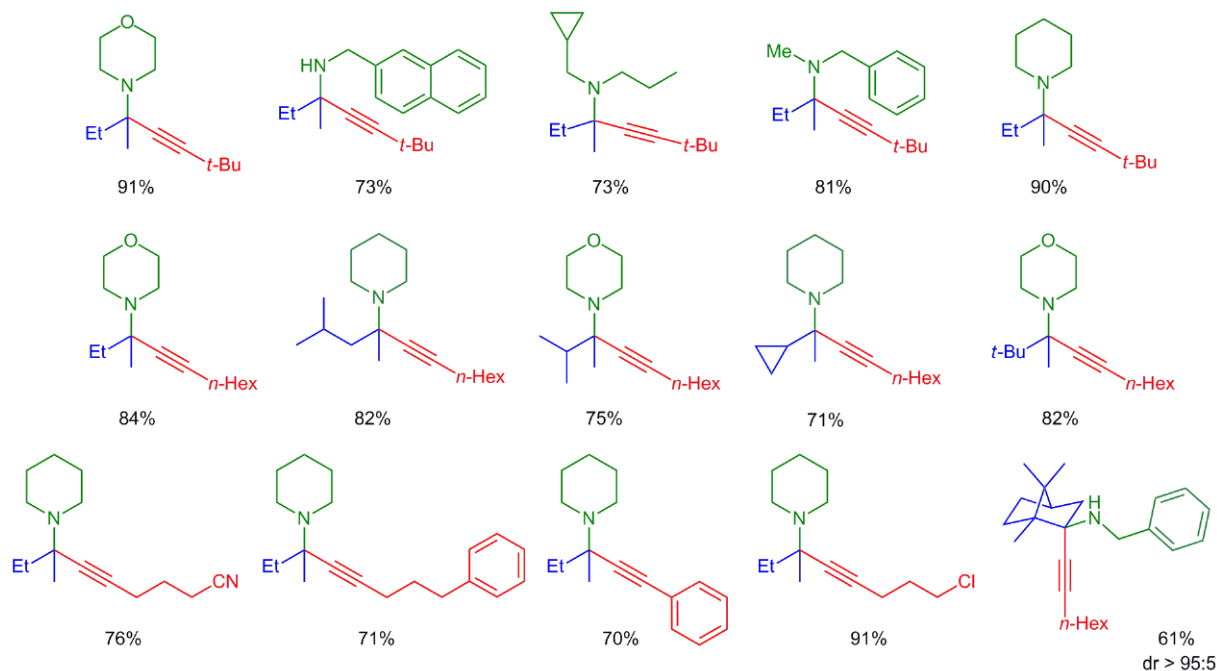
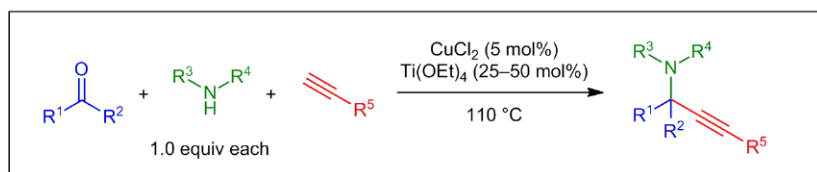
She continued: “Surprisingly, the reactivity bridge between aldehydes and cyclohexanone is drastically smaller than the gulf between cyclohexanone and acyclic ketones.” Whereas an aldehyde reacts at only twice the rate of cyclohexanone

under the same copper(II) triflate conditions,⁵ unactivated acyclic ketones were completely unproductive. Professor Larsen explained: “The critical turning point arose from our investigations into a greener solvent-free system to generate symmetric fully substituted propargylamines.” Graduate student Conor Pierce had found that inexpensive copper(II) chloride allowed for the 3CC of equimolar amounts of cyclohexanone,⁶ a range of amines, and terminal alkynes. Ellman and co-workers⁷ and the group of Davis⁸ showed that two to five equivalents of titanium(IV) ethoxide, which is a Lewis acid, was effective at cleanly generating ketimines from a ketone and an amine. “Testing the efficacy of Lewis acids as additives under our own CuCl₂ conditions showed that the addition of catalytic rather than stoichiometric amounts of Ti(OEt)₄ provides superior conversion into tetrasubstituted propargylamines via ketimine intermediates,” said Professor Larsen. “To our delight, this dual copper/titanium catalyst system provides direct access to a range of novel compounds containing tetrasubstituted carbon centers.” As a bonus, this groundbreaking method was developed from a platform of green chemistry: no solvents or wasted starting materials, such that the only by-product is one equivalent of water.

The rate of the 3CC with both Cu(II) and Ti(IV) is twice the rate of the alkynylation of isolated ketimine in the presence of only Cu(II). Since the ketone–amine–alkyne coupling is relatively insensitive to up to five equivalents of water, it seems less likely that the equivalent of water condensed during the 3CC is the origin of its faster rate. The exact mechanism of action of this dual catalyst system is still being determined.

“The next logical step is to develop an enantioselective variant,” said Professor Larsen. This is a daunting task, as currently the best result for the analogous ketone–amine–cyanide Strecker coupling appears to be 40% ee.⁹ Again, this highlights the difficulties associated with the 3CC compared to the attack on pre-synthesized ketimine. Enantioselective additions of nucleophiles to ketimines have resulted in dozens of





top-tier communications, but the work of Jacobsen and Vallee to develop the asymmetric Strecker coupling of ketimines¹⁰ preceded Prakash's and Olah's racemic 3CC Strecker coupling by seven years.² "Given these problems, this unexplored area carries the potential for a lifetime of research in the formation of highly substituted carbons bearing amines," remarked Professor Larsen. "Our interest in nitrogen-containing compounds is also displayed in the three other areas in which my lab is producing novel synthetic methods: heteroarenes, organometallic complexes, and a new class of pyrrole-based asymmetric ligands."

Graduate student Conor Pierce and undergraduate Mary Nguyen are expanding this method to other nucleophiles, and Conor is also working on asymmetric variants. Professor Larsen concluded: "We have introduced the second successful type of nucleophile to directly access these tetrasubstituted carbons bearing amines directly from ketones. As a Southern California native, I would translate that last statement into 'We are always happy to be introducing cool chemistry!'"

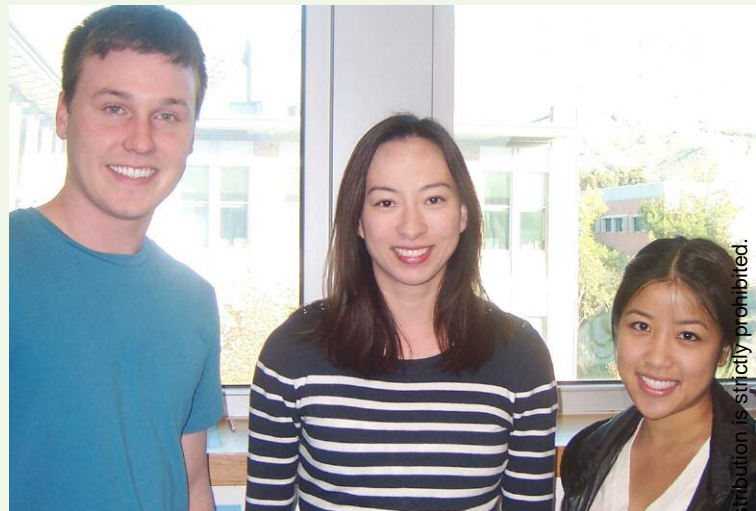
Matteo Zanda

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About the authors



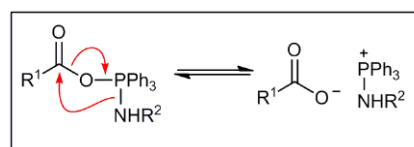
From left: C. J. Pierce, Prof. C. H. Larsen, M. Nguyen

Phosphine-Based Redox Catalysis in the Direct Traceless Staudinger Ligation of Carboxylic Acids and Azides

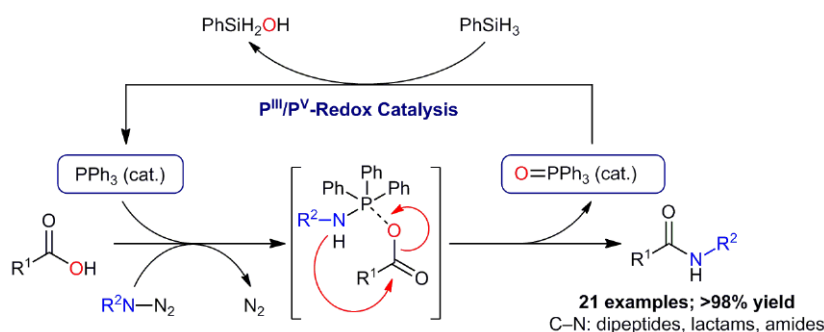
Angew. Chem. Int. Ed. **2012**, *51*, 12036–12040

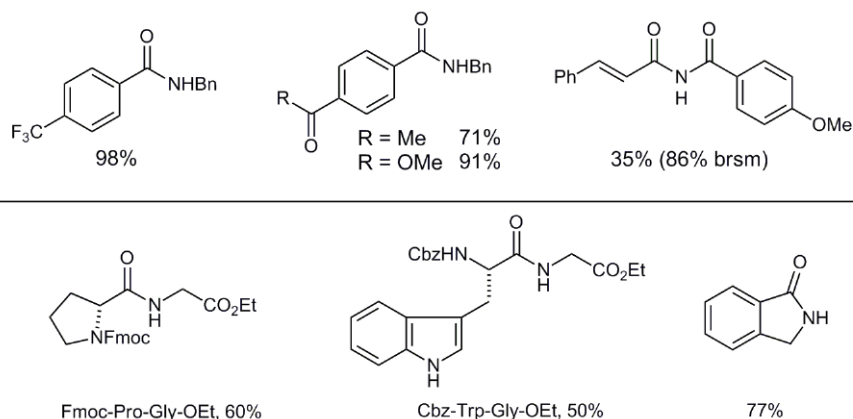
■ The interconversion of carboxylic acid derivatives through nucleophilic acyl substitutions represents one of the most fundamental transformations in synthetic organic chemistry. One of the most widely utilized strategies for functionalization involves the dehydration of carboxylic acids via an activated acyl intermediate. Unfortunately, difficulties with product purification, the need for oftentimes caustic reagents, generally acidic conditions, and poor atom-economy of the dehydration process are several of the drawbacks to this approach. To address these issues, recent efforts in Brandon Ashfeld's research group at the University of Notre Dame (Indiana, USA) have focused on the development of alternative catalytic dehydration methods, as well as on the direct use of carboxylic acids as substrates for this transformation. Dr. Ashfeld said: "In previous work, we have advanced a new Staudinger-type ligation strategy using chlorophosphites for the construction of amides and lactams from carboxylic acids and azides.¹ By using chlorophosphites, analytically pure products can be obtained following a simple aqueous work-up to remove the corresponding phosphinic acid." However, despite rectifying the issues of purification and harsh reagents, poor atom-economy remained in effect during the nucleophilic acyl substitution event. Dr. Ashfeld explained: "Inspired by recent developments in redox phosphorus-catalyzed transformations, including the Wittig,² Appel,^{3,4} and Staudinger reduction,⁵ we envisioned a conceptually new approach toward the phosphine-catalyzed Staudinger ligation, in which carboxylic acids are directly converted into amides through a P(III)/P(V)-redox-driven cycle."

Unlike the conventional Staudinger ligation, wherein $R_3P=O$ is generated by hydrolysis of an amidophosphonium salt, a catalytic variant would require oxygen transfer from the carboxylic acid to the phosphorus under anhydrous conditions. Dr. Ashfeld explained: "A key component of the catalytic variant relies on a phosphonium carboxylate-type intermediate, resulting from the acid–base reaction between the aza-ylide intermediate and carboxylic acid."

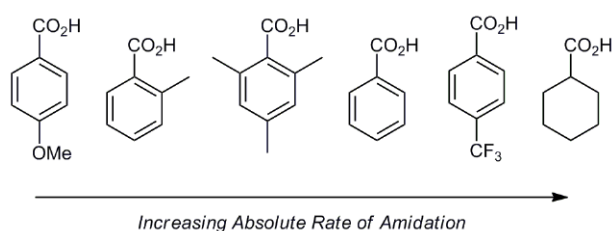


He continued: "Overall, the treatment of various carboxylic acids with a diverse array of azides provided amides in good to excellent yields with the use of catalytic PPh_3 (10 mol%) and $PhSiH_3$." A graduate student in his group, Andrew Kosal, carried out experimental work on chiral amino acid derivatives and found that dipeptides were produced in good yields with no evidence of racemization. Most notable was the synthesis of the Cbz-Trp-Gly-OEt dipeptide in which the reaction proceeded without protection of the indole nitrogen. "As current peptide syntheses require wasteful protection and deprotection strategies, this method could potentially provide a more atom-economical approach toward peptide synthesis," said Dr. Ashfeld.





Erin Wilson, a fourth-year graduate student at Notre Dame, played an instrumental role in determining what steric or electronic factors within the carboxylic acid component had on the absolute rate of the amidation event. Unreacted carboxylic acid was observed by quenching aliquots with diazomethane to produce the methyl ester, which was completely soluble in deuterated acetone used for these NMR experiments. Dr. Ashfeld said: “Using an internal standard, the amounts of ester (corresponding to starting material) and amide product were observed in the ^1H NMR spectra. These NMR experiments offered support that a tighter binding of the carboxylate to the phosphonium ylide resulted in a faster absolute rate of O-to-N acyl migration.”



The authors explained that this report describes the first phosphine-catalyzed Staudinger-type ligation that enables the direct conversion of carboxylic acids into amides while avoiding complications associated with preactivation and isolation due to stoichiometric phosphine oxide. Dr. Ashfeld concluded: “This method allows for access to an assortment of amides through the direct functionalization of carboxylic acids utilizing azides. The phosphine redox catalytic cycle constitutes a conceptually new approach toward amide bond formations via

an unusual intramolecular acyl migration. This strategy of catalytic acyl activation toward C–N bond formation has the potential for broad applicability in the construction of valuable synthetic building blocks.”

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About the authors



A. Kosal

Andy Kosal was born in Midland, Michigan (USA) in 1985. He received his B.Sc. in chemistry from Alma College (USA) while researching bis-annulated benzene rings under the direction of Dr. Robert Burns. He is in the process of completing his Ph.D. at the University of Notre Dame (USA) under the direction of Dr. Brandon L. Ashfeld. Andy carried out the optimization and substrate scope experiments.



E. E. Wilson

Erin Wilson was born in Conway, South Carolina (USA) in 1987. She received her B.Sc. in chemistry at Winthrop University (Rock Hill, SC, USA) where she researched new targets for sphingosine kinase 1 inhibitors under the guidance of Dr. Thomas Grattan. She is currently pursuing her Ph.D. degree under the supervision of Dr. Brandon Ashfeld at the University of Notre Dame (USA).

She carried out the absolute rate studies, as well as a portion of the optimization, competition studies, and substrate scope experiments.



Prof. B. L. Ashfeld

Brandon Ashfeld was born in Minnesota (USA) and received his B.Sc. degree in chemistry from the University of Minnesota–Twin Cities (USA) in 1998 while working in the laboratories of Professor Thomas R. Hoye. In the autumn of 1999 he enrolled in graduate studies at the University of Texas at Austin (USA) and received his Ph.D. under the supervision of Professor Stephen F. Martin in 2004. He then moved to

Stanford University (USA) and joined the laboratories of Professor Barry M. Trost as a National Institutes of Health Ruth L. Kirschstein postdoctoral fellow. In the autumn of 2007 he joined the faculty in the Department of Chemistry and Biochemistry at the University of Notre Dame where his research program is focused on the development of new bifunctional transition-metal-catalyzed methods for the convergent assembly of biologically active natural products, the modification and evaluation of these synthetic targets for brain and nervous system cancer cytotoxicity, and the identification, design and synthesis of small-molecule N-heterocycles as ionic liquid precursors for the efficient gas-phase separation of CO₂.

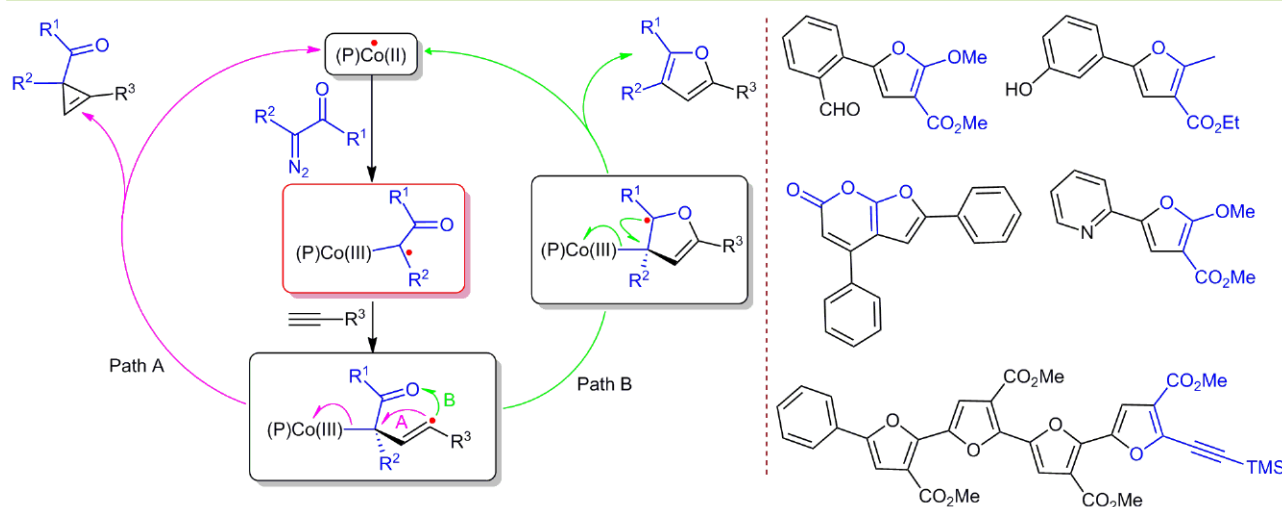
Regioselective Synthesis of Multisubstituted Furans via Metalloradical Cyclization of Alkynes with α -Diazocarbonyls: Construction of Functionalized α -Oligofurans

J. Am. Chem. Soc. **2012**, *134*, 19981–19984

The furan ring is present in a broad range of natural and/or bioactive molecules; furthermore, it constitutes a versatile synthetic building block susceptible to both reduction and oxidation reactions, as well as to a variety of ring-opening processes. Although the first synthesis of a furan dates back to 1780 (2-furoic acid), the synthesis of complex molecules containing the furan ring continues to represent a very active and stimulating area of organic chemistry. One conceptually novel strategy for the synthesis of highly functionalized furans, as well as oligofurans, has recently been reported by the research group of Professor Peter Zhang at the University of South Florida (Tampa, USA). Professor Zhang and co-workers are using stable metalloradicals with well-defined open-shell doublet d^7 electronic structure, such as cobalt(II) complexes of porphyrins {[Co(Por)]}, as metalloradical catalysts for stereo-selective radical reactions. This concept of metalloradical catalysis (MRC) provides a catalytic approach for the generation of C- and N-based radicals as well as the control of reactivity and selectivity of subsequent reactions of these radical intermediates. As the first demonstration of MRC for stereo-

selective radical synthesis, [Co(Por)] have been developed as a new class of effective chiral catalysts for the asymmetric cyclopropanation of alkenes, allowing the Tampa-based researchers to address several long-standing issues in the field (*Angew. Chem. Int. Ed.* **2009**, *48*, 850). Professor Zhang said: “Mechanistic studies have demonstrated that [Co(Por)]-catalyzed cyclopropanation operates with an unprecedented catalytic mechanism involving an unusual Co(III)-carbene radical as the key intermediate, followed by stepwise radical addition-substitution pathway (*J. Am. Chem. Soc.* **2010**, *132*, 10891; *J. Am. Chem. Soc.* **2011**, *133*, 8518).” He continued: “As another application of Co(II)-based MRC for different unsaturated substrates, [Co(Por)] have been shown to be effective catalysts for the enantioselective cyclopropanation of alkynes (Scheme 1, Path A; *J. Am. Chem. Soc.* **2011**, *133*, 3304).”

To further explore the application of MRC for other radical cyclization reactions, Professor Zhang and his group demonstrated in the featured paper that the Co(II)-catalyzed radical cyclization of alkynes with diazo reagents can be completely

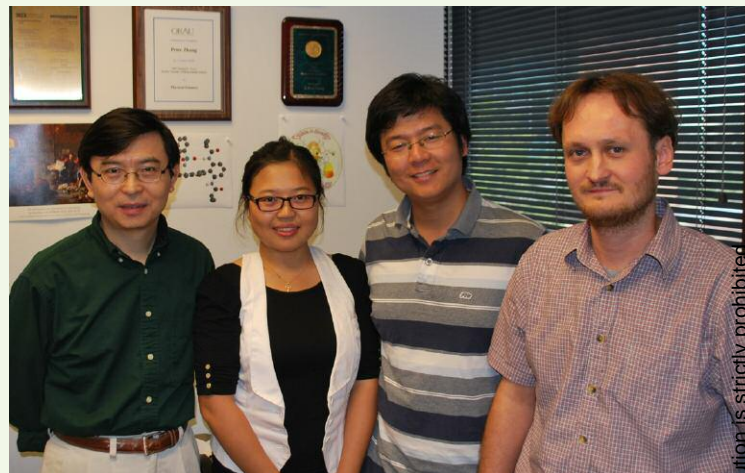


Scheme 1 Synthesis of multisubstituted furans and α -oligofurans via radical cyclization of alkynes with α -diazocarbonyls by Co(II)-based metalloradical catalysis

switched from previously reported cyclopropanation (Scheme 1, Path A) to furan formation (Scheme 1, Path B) through judicious use of diazo reagents and fine-tuning of the catalytic conditions. Professor Zhang said: “[Co(Por)] have been shown to be general catalysts for the effective synthesis of polyfunctionalized furans through intermolecular radical cyclization of various acetylenes with α -diazocarbonyls. This radical cyclization process by [Co(Por)], which is mechanistically different from previous systems, is suitable for different kinds of α -diazocarbonyls and terminal acetylenes with varied electronic properties.” In addition to its broad substrate scope and excellent regioselectivity, the Co(II)-catalyzed furan synthesis features an unusual degree of functional group tolerance, allowing for the direct preparation of furan derivatives containing various functionalities, such as NR₂, CHO, and OH groups (Scheme 1). Further applications of the Co(II)-based metalloradical cyclization have been successfully demonstrated for the construction of O-biheterocycles and functionalized α -oligofurans through double and iterative radical cyclization processes, respectively (Scheme 1). Professor Zhang concluded: “This new Co(II)-based radical cyclization process implies an unprecedented tandem radical addition pathway of Co(III)-carbene radicals with the involvement of neighboring carbonyl groups, leading to the synthesis of five-membered rings rather than the previously reported three-membered rings. As such, it broadens the applications of the concept of MRC for the syntheses of cyclic compounds with ring sizes beyond the established three-membered rings.” ■

Matteo Zanda

About the authors



From left: Prof. P. Zhang, Dr. X. Xu, Dr. X. Cui, Dr. L. Wojtas

Peter Zhang received his Ph.D. degree in chemistry from the University of Pennsylvania (USA) in 1996, where he carried out research work on a Rh(II)-based system for the activation of methane and carbon monoxide under the direction of Professor Bradford Wayland. He then undertook postdoctoral work at the Massachusetts Institute of Technology (Cambridge, USA) as a National Institutes of Health (NIH) Postdoctoral Fellow during the period of 1996–2001, first with Professor Stephen Lippard on the construction of functional models for methane monooxygenase (MMO) and then with Professor Stephen Buchwald on the synthesis of polyanilines (PANIs) via Pd-catalyzed amination. Professor Zhang began his independent career as Assistant Professor of Chemistry at the University of Tennessee (Knoxville, USA) in 2001. He joined the University of South Florida as Associate Professor of Chemistry in 2006 and was promoted to Professor of Chemistry in 2010. Professor Zhang's research and education activities have been recognized with several awards, including the NSF CAREER Award.

Xin Cui received his Ph.D. degree in chemistry from the University of Science and Technology of China (Hefei, P. R. of China) in 2008, where he carried out research work on phosphine-free Pd-catalyzed cross-coupling reactions and synthesis of heterocycles under the supervision of Professor Qingxiang Guo. During the period of 2008–2012, he performed his postdoctoral research with Professor Peter Zhang at the University of South Florida. He is currently a Research Assistant Professor in the research group of Professor Zhang. His current research is mainly devoted to asymmetric cyclopropanation and C–H functionalization by Co(II)-based metalloradical catalysis and their applications for stereoselective organic synthesis.

Young Career Focus: Professor Jimmy Wu (Dartmouth College, Hanover, NH, USA)

■ **Background and Purpose.** *SYNFORM* will from time to time meet young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This *SYNSTORY* with a **Young Career Focus** presents Professor Jimmy Wu, Dartmouth College, Hanover, NH, USA.

BIOGRAPHICAL SKETCH



Prof. J. Wu

Jimmy Wu was born in Taiwan in 1976. He received his A.B. degree in Chemistry from Princeton University (USA) in 1998. He then spent two years as an associate chemist at Merck Process Research (USA) where he worked on the development of selective COX-II inhibitors. Afterwards, he moved to Harvard University (USA) where he obtained his PhD in organic chemistry from Professor

David A. Evans. His doctoral work focused on asymmetric catalysis using lanthanide-pybox complexes. He continued his studies as a postdoctoral fellow with Professor Barry M. Trost at Stanford University (USA) where he worked on the synthesis of indoline alkaloid communesin B. He joined the Department of Chemistry at Dartmouth College (USA) in the summer of 2007.

INTERVIEW

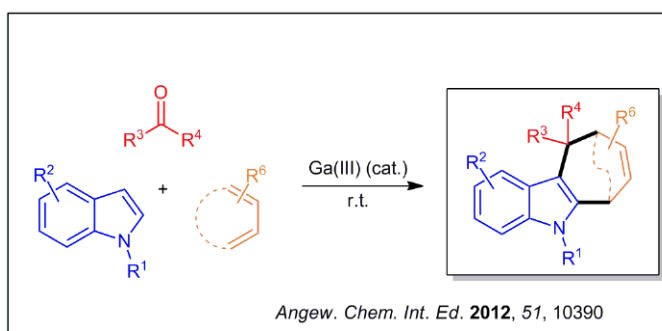
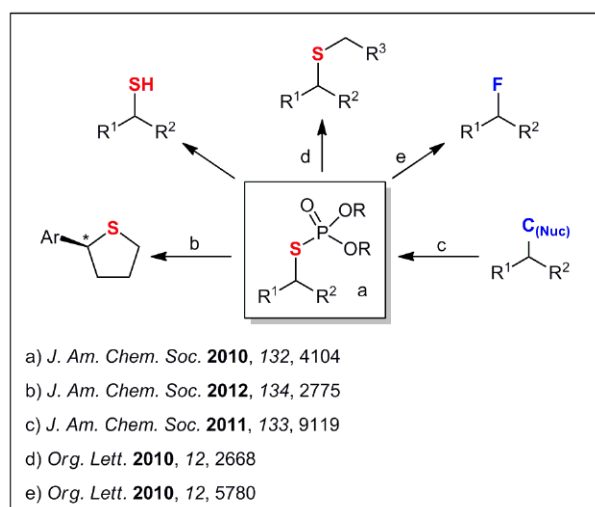
SYNFORM | *What is the focus of your current research activity?*

Prof. Jimmy Wu | My research can be roughly divided into two major programmatic themes. The first of these focuses on the discovery of new methodologies for the construction of carbon-sulfur bonds. Sulfur is an integral (but under-appreciated) component of pharmaceutical drugs. Despite the prominence of sulfur in medicine and other fields, the synthetic methods by which it is incorporated into molecules are limited in both breadth and scope. A brief survey of organosulfur chemistry reveals that it lags substantially behind the many exciting technologies being developed for carbon, nitrogen, and oxygen. A long-term goal of my group is to modernize the study of sulfur by the rational and systematic application of contemporary chemical theory to the design of new reactions involving this element.

The second major research thrust in my group concentrates on the discovery of new alkylation and annulation strategies for indoles and related heterocycles. Heterocyclic compounds are ubiquitous in nature and medicine and are even more prevalent than sulfur in active therapeutic agents. Indole is arguably one of the most important heterocycles in medicine; but, despite nearly a century of research, numerous synthetic challenges remain unresolved.

SYNFORM | *When did you get interested in synthesis?*

Prof. Jimmy Wu | As I'm sure is the case with many other scientists, my interest in synthesis began with a handful of fantastic teachers and mentors. During my undergraduate studies, it was Marty Semmelhack and Mait Jones who first introduced me to the wonderful world of organic chemistry. But it was during my time as a bachelor level chemist at Merck Process Research when I realized that graduate school was in my future. At Merck, I witnessed firsthand what organic chemistry could do for society. What a thrill it was for a young man like me, fresh out of university, to be given the opportunity to make meaningful contributions to human health! I entered graduate school with grand plans of one day establishing my own academic research program.



My PhD and postdoctoral advisors (David Evans and Barry Trost, respectively) provided me with the tools to do just that.

SYNFORM | *What do you think about the modern role and prospects of organic synthesis?*

Prof. Jimmy Wu | As synthetic chemists, we have the unique ability to make molecules, both natural and unnatural ones. We can do this better and more efficiently than at any other time in history. We continue to develop, at an incredible rate, breathtaking new methodologies that enable the synthesis of very complex molecules. By reaching out to our colleagues in other fields, we have a chance to redefine the boundaries of scientific disciplines. We should try to establish meaningful collaborations as best we can and be accepting of new opportunities as they are presented to us. In my opinion, this is how we as organic chemists will make the biggest scientific impact.

SYNFORM | *Your research group is active in the area of sulfur organic chemistry and metal-mediated synthesis. Could you tell us more about your research and aims?*

Prof. Jimmy Wu | My group has developed several new technologies for constructing carbon–sulfur bonds. For instance, we reported methods for the direct displacement of alcohols and/or other oxygen-based leaving groups using catalytic Ga(OTf)₃ or UV light. The products of these transformations are phosphorothioate esters (and other thioethers). These are versatile functional groups that can be further con-

verted into thiols, thioethers, and enantioenriched tetrahydrothiophenes. We have also demonstrated that allylic phosphorothioate esters readily participate in transition-metal-catalyzed cross-coupling reactions with fluoride and a diverse range of Grignard reagents to furnish carbon–fluorine and carbon–carbon bonds.

More recently, our group has reported Ga(III)-catalyzed three-component annulation strategies to generate cyclohepta[b]indoles. This is an important class of compounds which has garnered considerable interest from the chemical community as potential therapeutics.

SYNFORM | *What is your most important scientific achievement to date and why?*

Prof. Jimmy Wu | It is an honor to even be asked this question; however, I think it is perhaps up to the scientific community to judge what has been our most important achievement to date.

Matteo Zanda

COMING SOON ► ► COMING SOON ► ►

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SYNSTORIES ■ ■ ■ ■

■ Taming of Fluoroform: Direct Nucleophilic Trifluoromethylation of Si, B, S, and C Centers

(Focus on an article from the current literature)

■ Catalytic Enantioselective Allylic Amination of Unactivated Terminal Olefins via an Ene Reaction/[2,3]-Rearrangement

(Focus on an article from the current literature)

■ A Chiral Cage-like Copper(I) Catalyst for the Highly Enantioselective Synthesis of 1,1-Cyclopropane Diesters

(Focus on an article from the current literature)

FURTHER HIGHLIGHTS + + + +

SYNTHESIS

Review on: Iodine in Modern Oxidation Catalysis

(by B. Nachtsheim)

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Account on: Catalytic Ring Expansion Adventures

(by J. T. Njardarson)

SYNFACTS

Synfact of the Month in category "Metal-Mediated Synthesis":

[Ni-Catalyzed Suzuki Arylation of Unactivated Tertiary Alkyl Halides](#)

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