

Organometallics Roundtable 2013–2014

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ABSTRACT: A panel of seventeen experts from academia, industry, and government laboratories share their thoughts on a variety of matters of importance to the readership of *Organometallics*. These include directions for the field and recent breakthroughs (illustrated with selected examples), the interface with green chemistry, the quest for reproducible experimental procedures, data and research integrity, laboratory safety, the preparation of coworkers for non-academic careers, and needs regarding instrumentation, infrastructure, shared facilities, and computational methods. A lively give and take is evident in the edited transcript, which continues a biennial tradition initiated in 2011.



The discipline of chemistry has never seen a period of greater change. Academic institutions are evolving the way they teach chemistry at all levels. Industrial institutions that go back decades or even centuries continue to downsize and/or divest, with respect to both research and manufacturing. However, a variety of younger entities, including many “startups”, have found opportunity in the resulting void. Scientific publishing is witnessing a veritable revolution, with content being delivered through multiple channels that were beyond anyone’s imagination a generation ago. Meanwhile, regulations and guidelines multiply unabated, impacting chemistry workplaces in all countries. These trends send regular series of ripples and tidal waves through graduate research in academic institutions. What’s a reader of this journal to do?

Fortunately, the pulse of organometallic chemistry continues to beat strongly, as judged by the 2013–2014 “*Organometallics* Roundtable” that follows. This represents the second installment of a “tradition” established in 2011, when 17 panelists from industry, academia, and points around the world met at the Denver ACS meeting (August 2011) for the first “*Organometallics* Roundtable”. The journal is fortunate that so many busy experts could again take the time to spend with us, on



A portion of the panel in action.

this occasion at the Indianapolis ACS meeting (September 2013). The following pages constitute an edited transcript of the ensuing discussion, which was structured around the nine questions summarized in the side bar and repeated below. It is hoped that these pages concisely frame both the opportunities and challenges facing organometallic chemistry in the years ahead. ***Organometallics:* Suppose the New Year could bring you one new reaction or process that would greatly help with an organometallic problem in your own research. What would be your wish?**

Patrick Holland: Many organometallic chemists like myself aim to make bulky ligands that modulate the reactivity of a metal. However, this requires the formation of bonds in very crowded environments. Thus, coupling reactions that are tolerant to hindered substrates would be very useful for us. Such enabling technologies would allow us to make a broader range of ligands to control the reactivities of metals (see Figure 1 for two useful, recently reported, bulky phosphine ligands).^{1a,b}

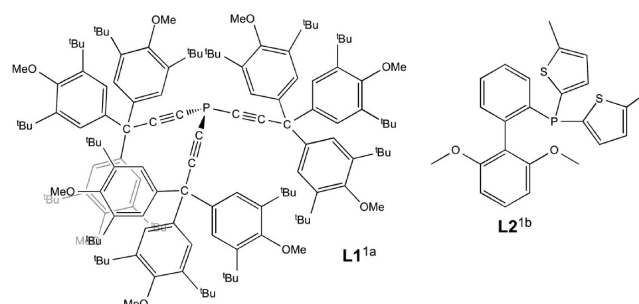


Figure 1.

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Don Tilley: Many organometallic chemists are trying to design catalysts that are more active and/or more selective. Invariably, this involves design and synthesis of new ligands, and the construction of these ligands is in general a synthetic challenge. Often one uses coupling reactions in order to install large groups into nitrogen- or phosphorus-based ligands. But just in terms of phosphorus chemistry there are limited ways to make phosphorus–carbon bonds and carry out substitutions at phosphorus that allow introduction of phosphorus-based units into a ligand framework. So I agree that ligand synthesis remains a huge problem for the field.

Christina White: I still feel like there is not a very good understanding on how the ligand environment affects reactivity, even though we've come a long way on many subjects. Consider the amazing chemistry that goes on in metalloenzymes. We know a lot about the coordination sphere for enzymes like methane monooxygenase,² and with small molecule mimics there's been some beautiful work where many of the spectroscopic features of the enzyme have been replicated. However, these related nonheme iron model complexes cannot reproduce the chemistry of the enzyme. I find the disconnect between the ability to replicate the spectroscopic features but not the enzymatic chemistry to be fascinating. Alternatively, there are nonheme iron complexes that can effect oxidations of strong secondary or tertiary carbon–hydrogen bonds that do not structurally or spectroscopically resemble nonheme enzymatic active sites at all (see Figure 15 below). Again, this sort of disconnect has always fascinated me and it would be tremendous if we could fully understand exactly how the ligand environment is impacting the chemistry that goes on in both the enzymes and the small-molecule systems.

Connie Lu: Regarding the disconnect between enzymes and their model complexes, I would use another “f” word, “frustrating”. I believe that it is important to learn from the failures in mimicking enzymatic active sites. So often, one reads the disappointing result without really understanding why the activity was not reproduced. I believe there is a bigger lesson to be learned from these failures, and we need theorists to help the experimentalists fill in these gaps.

Christina White: One reads this fascinating literature and thinks, “well, based on these spectroscopic studies maybe I can do this and that's going to improve things,” and it ends up being something completely different. Ultimately, it becomes an empirical exercise of trying a lot of different ligands to find the one that will support the desired reactivity.

Connie Lu: Yes, this is a limiting problem in the field of organometallics. Our understanding of reaction mechanisms does not capture everything these catalysts can do. How do we avoid nonproductive pathways? This would be a game changer for developing new catalysts.

Jack Norton: One of my interests is hydrogen and metal hydrides, and I would like to see us better able to interconvert hydrogen gas and metal hydrides, particularly those of the transition metals. This can be done well in a few cases but looks thermodynamically attractive (in one direction or the other) in many more. This interconversion is important in the generation of hydrogen from solar energy, as well as in the use of hydrogen as a feedstock.

Robin Bedford: One very popular theme today is the development of catalytic reactions involving Earth-abundant metals, particularly iron. If rapid, direct boron to iron transmetalation could be routinely realized, it might lead to major advances in iron-catalyzed cross-coupling chemistry and related borylation reactions. I was talking to Pat about this yesterday, he has one of the very few papers with genuine examples of direct boron to iron transmetalation reactions that proceed without the need for main-group-metal additives,³ but the reactions are quite slow. Reading



The panel debating the first question.

the literature one might assume, from proposed mechanisms, that this transmetalation step occurs easily, but I am not convinced. I think in many cases the main group salt “additives” may play a complex intermediary role and that this actually remains a major obstacle in developing new catalytic reactions based on iron.

Marina Petrukhina: Pat's points about ligand design resonate with just about everyone. We are working with nonplanar curved and strained polyaromatic systems. None of them are commercially available. So developing improved, scalable synthetic organic chemistry that would lead to these ligands would greatly help our efforts to exploit their organometallic, coordination, and materials chemistry. All of these remain poorly developed due to limitations on ligand quantities. It takes weeks and tons of money for us to even get milligram quantities of certain polyarenes. So this is a major challenge for us.

Edwin Webster: Since computational chemistry has been mentioned, let me chime in. Ground-state properties are the least computationally complex and are therefore easier to determine, but when you are talking about reactivity and any involvement of excited states, that is a huge challenge right now for any of the common methodologies. Linear free-energy relationships are also relatively easy. Regarding ligand design, I certainly understand that this is very complicated, and conformational flexibility becomes one of the biggest issues, because when you go to the bulkier and more complex ligands like Pat was talking about, it is more difficult because of the entropic contributions to the free energy. Sampling all of the conformational space and correctly including these terms is quite computationally expensive, and most people are not very systematic. They simply throw it in and say, “well, this is what the computer gave me; this is the answer,” and it is not, most of the time, the right answer for the right reason.

Karen Goldberg: In terms of new reactions and processes, I want to go back to an old, unsolved problem. This would be catalysts that would take methane to methanol, ethane, or essentially any functionalized or less volatile molecule. The amount of methane that is available now is enormous. This is something organometallic chemists were very interested in during the 1970s and 1980s. There has been a baseline of ongoing interest, but there is just so much more methane available now. There is a critical need for catalysts and solvents that will not degrade under oxygen or at high temperatures, and that will enable highly selective conversions of methane to other feedstocks in high yields.

Tong Ren: I want to make a couple of observations. You have been asking for a wish list, and to me we still do not have a highly robust photo-CO₂ reduction catalyst that gives high turnover numbers. The state of the art catalysts are, by and large, derived from the prototype Re(bipy)(CO)₃X catalysts put forward by Lehn in the early 1980s.⁴ Driven by the impetus of solar-based renewable energy research, especially hydrogen production from water splitting and carbon dioxide reduction, organometallic photochemistry is ripe for a renaissance.

Summary of Panel Questions

(1) Suppose the New Year could bring you one new reaction or process that would greatly help with an organometallic problem in your own research. What would be your wish?

(2) Let's shift from current needs to recent accomplishments. What comes to mind as some of the most impactful achievements in organometallic chemistry during 2012 and 2013? Please justify your selection.

(3) We've treated both the present and the past. Let's now consider the major future challenges that organometallic chemists should be trying to address in the next few years. What societal needs and fundamental questions deserve particular attention? Where should we be heading, and why?

(4) Green chemistry continues to expand as a discipline, and the ACS has recently launched a new journal that covers this field. Do you see this as an area of opportunity for organometallic chemists? Do organometallic chemists need to be more cognizant of the principles of green chemistry in their own research?

(5) Many in the synthetic chemistry community believe that journals should be able to provide more reproducible experimental procedures. What in your opinion are some of the obstacles and problems in this regard? Even with *Organic Synthesis*, 12% of the submitted procedures are typically found to be irreproducible.

(6) A recent Editorial by Amos Smith entitled "Data Integrity" stated that "research institutions ... need to create an environment that fosters research integrity through education, training, and mentoring and by embracing incentives that deter irresponsible actions". What can be done to help maintain the highest standards in organometallic chemistry? What should research advisors, reviewers, and editors be doing?

(7) One continues to read about accidents in academic research laboratories, and the well-publicized death of a researcher at UCLA involved an organometallic compound, *t*-BuLi. What are the implications for organometallic chemists? What could be improved in our approach to safety?

(8) In 2011, we discussed the advice we would give to co-workers beginning academic careers. For this Roundtable, let's discuss the preparation of co-workers for nonacademic careers, either in industry or as entrepreneurs. How can we be more effective, and how could academic and industrial chemists better work together?

(9) Let's return to the future of organometallic chemistry. To what extent do you perceive limitations based upon instrumentation, infrastructure, or shared facilities? Do any new (instrumental) techniques hold particular promise for breakthroughs? What role is computational chemistry currently playing?

François Gabbaï: As one of my wishes, I would like to be able to stabilize group 15-based cations in the +5 oxidation

state. In the past few years we have started to look at new types of Lewis acids such as phosphonium, arsonium, and stibonium. In a sense, we are revisiting some of the concepts proposed, or demonstrated, by George Olah, who used SbF_5 as a Lewis acid. However, our intent is to make organic versions of such Lewis acids and furthermore render them cationic to bring about even greater Lewis acidities (see Figure 2, left). A problem is that

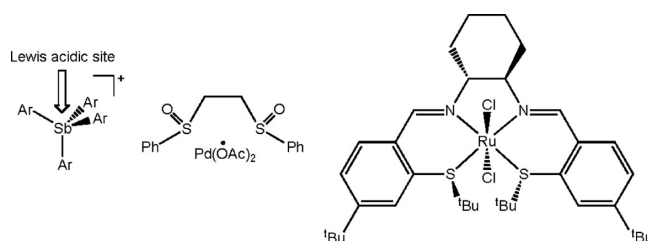


Figure 2.

these highly electron deficient systems are prone to reduction to the +3 oxidation state, thus compromising the Lewis acidity of the group 15 center. For this reason, it would really help me and my co-workers if there were ways to stabilize these highly oxidized and very electron deficient group 15 cations.

Shannon Stahl: I have a variety of interests in oxidation chemistry, and we have a dearth of versatile ligands for oxidation chemistry. This has many contexts. In organometallic oxidations of the type we are pursuing, the problem is ligands intrinsically attenuate the oxidizing ability of the metal. We lack access to what would be equivalent to a soft ligand—one that is not oxidizable or reactive like an olefin or phosphine. There are other domains, including molecular water oxidation catalysis and selective oxidations using hydrogen peroxide. It seems like we are stuck with pyridine and related heterocycles that are not as modular as phosphines. Amine ligands tend to get oxidized more readily, and polydentate nitrogen donor ligands such as phthalocyanines limit the number of vacant coordination sites. The entire topic of ligand structures for oxidation chemistry is an immense need and constitutes a major challenge for the field.

Christina White: Shannon, that is a very insightful comment, and it is particularly problematic with palladium. We work with palladium allylic oxidations, and we've developed a bis(sulfoxide) $\text{Pd}(\text{OAc})_2$ catalyst (see Figure 2, middle).⁵ However, we know from mechanistic studies that the sulfoxide is coming on and off the metal throughout the catalytic cycle. Because of this, the ligand is not highly effective at preventing $\text{Pd}(0)$ aggregation and plating prior to the requisite reoxidation back to palladium(II). Phosphine ligands would be better at preserving the palladium; however, they are not oxidatively stable. We are working on developing systems to lower the palladium loadings, but in general oxidative processes suffer from significantly higher loadings than reductive systems that can use phosphine ligands. For much of iron oxidation chemistry, the metal stays attached to the ligand, which prevents ligand oxidation, even with amines and pyridines. For example, with our $\text{Fe}(\text{PDP})$ catalyst (see Figure 15 below) for aliphatic carbon hydrogen bond oxidations, we can recover >90% of the PDP ligand untouched from the reaction. Unlike the traditional porphyrin ligands, the nonheme PDP ligand has two open coordination sites available to do chemistry.

Greg Whiteker: I'd like to follow up on the comment about synthetic methods for bulky phosphorus-containing ligands (Figure 1). There are some great ligands of these types out there for doing a wide variety of cross-coupling reactions. Those are

really useful on a discovery scale in medicinal chemistry. However, as an industrial chemist who tries to apply this chemistry in the synthesis of molecules on multiton scales, the costs of these ligands often outweigh the costs of the precious metals used for the catalyst. We do have ways to recycle and reclaim parts of the catalyst mixture. Nonetheless, very complicated and sophisticated ligands that are hard to synthesize limit the utility of catalyst systems on large scales.

Michael Krische: There's a recent report by Firmenich,⁶ a flavor-fragrance company, of a chiral sulfur-containing ligand for ruthenium-catalyzed ketone hydrogenation (see Figure 2, right). It is so deeply entrenched in conventional wisdom that phosphorus(III) ligands are required for efficient catalysis that one may neglect to consider sulfides, which are far less expensive; Firmenich must make many of their products for pennies on the kilo. Other approaches to asymmetric catalysis that continue to gain traction include the use of metals that are modified by chiral counteranions. These may prove especially useful in the context of oxidation catalysis, as phosphorus(III) and sulfur(II) ligands are not oxidatively stable.

Makoto Fujita: Of course, ligand design is very important in developing organometallic chemistry, but in my group we are interested in designing cavities and pockets, in other words "empty space" of a "tailored" nature. This is a totally new approach to control organometallic reactivity. In a related vein, new reactions of organometallic species have been developed in the cavities of MOFs and related cage structures. We also have observed new reactions and types of transformations in our metal templated polyhedral cages. Furthermore, consider Mother Nature's approach. All enzymatic reactions represent events in enzyme cavities, and therefore the design of synthetic cavities should constitute an interesting and productive strategy for developing new transformations.

Organometallics: Let's shift from current needs to recent accomplishments. What comes to mind as some of the most impactful achievements in organometallic chemistry during 2012 and 2013? Please justify your selection.

Jaqueline Kiplinger: I'd like to begin this discussion at the bottom of the periodic table. Some of the most important breakthroughs have their origins in systems that were studied around 20 years ago. Polly Arnold and Marinella Mazzanti have taken long known uranium(III) alkoxides and amides and discovered that they have profound reactivity with small molecules such as CO, CO₂, and nitrogen (see Figures 3 and 4).^{7,8} In particular, they have

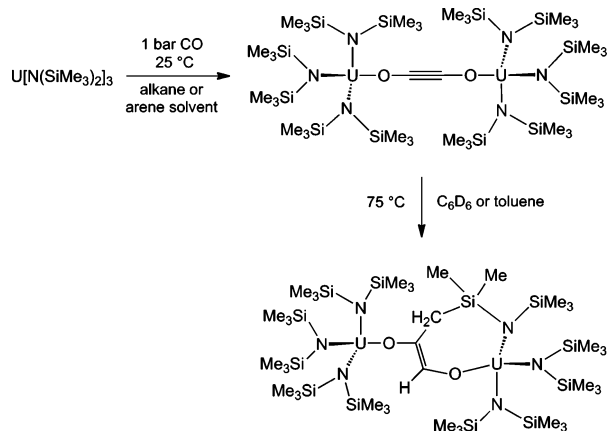


Figure 3.

studied the chemistry of these compounds in nonpolar solvents and found a world of reactivity that was simply missed earlier.

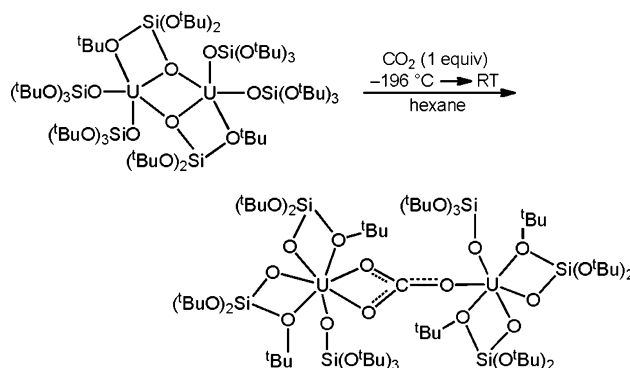


Figure 4.

In my opinion, there are abundant opportunities in returning to older, simpler systems and, with modern instrumentation and techniques, making really big discoveries.

Karen Goldberg: I'm a big fan of the recent work that has been done on taking CO₂ to methanol in homogeneous systems. There's Sanford's⁹ system in which she uses a tandem series of catalysts (see Figure 5) and Klankermayer and Leitner's¹⁰ ruthenium phosphine catalyst (see Figure 6). This is some of the most important C₁ chemistry being looked at today.

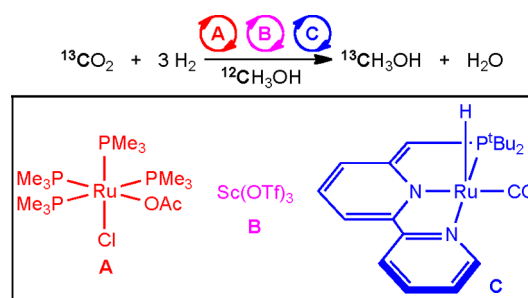


Figure 5.

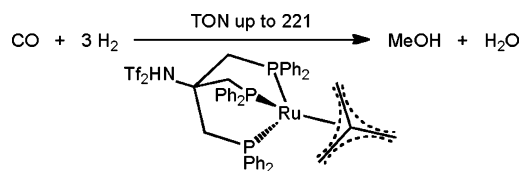


Figure 6.

Jack Norton: What bothers me here is the thermodynamics. CO₂ is a very stable molecule, "downhill" from virtually everything else. Can you convince me this is really going to revolutionize chemistry?

Karen Goldberg: With the increasing availability of solar energy, one has the means to drive and also scale up endergonic reactions. And with CO₂, there is always the recycling aspect.

Jack Norton: But one potentially has to put an enormous amount of energy in per molecule. I love it as a piece of pure science, but I worry about the numbers.

Robin Bedford: I think the point being made is if it is sunlight driven, the amount of energy per molecule really does not matter. In the right parts of the world, one has abundant sunlight.

Karen Goldberg: Exactly.

Shannon Stahl: One topic that has been expanding significantly is "second coordination sphere control" over reactivity and selectivity. The work that is going on with nickel complexes of

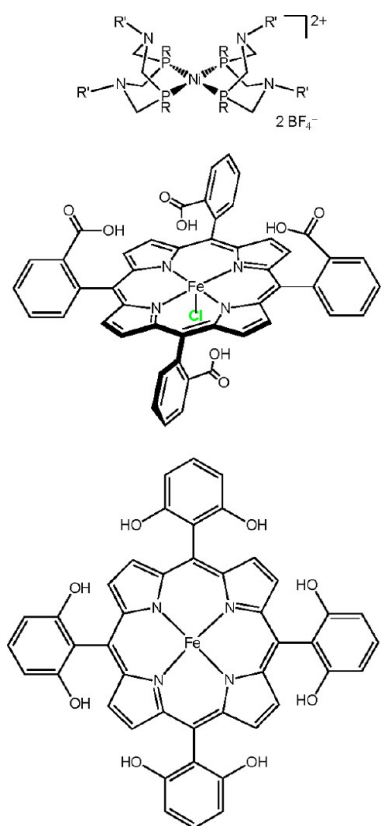


Figure 7.

amine-containing diphosphine ligands at PNNL has boggled my mind (see Figure 7, top).¹¹ And the initial results involving electrocatalytic H_2 formation have been extended to dinitrogen activation.¹² In a related vein is Jim Mayer's work with O_2 reduction,¹³ and Savéant's work with CO_2 chemistry,¹⁴ all involving secondary coordination sphere interactions (see Figure 7, middle and bottom). It seems like these developments could really transform the field of organometallic chemistry and molecular catalysis.

Don Tilley: Speaking of nitrogen, I have been impressed with Jonas Peters' recent work on nitrogen reduction. Some of the inspiration for this came from evidence for carbon in the iron coordination sphere of a nitrogenase enzyme. Peters and his group have attempted to prepare functional models, first with boron,¹⁵ but then they discovered nitrogen reduction

with a related "iron-only" species. They are now investigating a number of extensions, including model compounds with carbon (see Figure 8). To me, there is a lot of insight and creativity in these fundamental advances.

Patrick Holland: I completely concur. Like Don just mentioned, it has only been about 2 years since it was discovered that the FeMoco, the active site of nitrogenase, has a carbide at the center (see Figure 9, top).¹⁶ Since the FeMoco

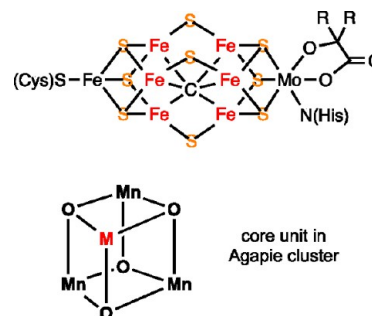


Figure 9.

has six iron–carbon bonds, we can definitely view nitrogenase as an organometallic molecule now. However, it is not yet clear how this structural feature is related to the mechanism. Maybe it is there for stability, or perhaps it is a hemilabile ligand. This is going to be a fascinating subject going into the future.

François Gabbai: I want to balance out the transition-metal and actinide chemistry with comments regarding the main-group sector. First, in the context of CO_2 reduction, there has also been beautiful work carried out with boron,¹⁷ aluminum,¹⁸ and silicon¹⁹ Lewis acids. Some of the players here include Erker,^{17a,20} Fontaine,^{17c,18c,21} Lammertsma,^{18b,e} Müller,^{19b,22} O'Hare,^{17b} Piers,^{19a} Stephan,^{17a,18a,23} Uhl,^{18b,e} and Wehmschulte.^{18d,f} Second, I'd like to emphasize that—as noted in passing by Don Tilley—boron is present in some increasingly popular ligands such as those pioneered by Didier Bourissou²⁴ and recently used by Peters in iron complexes that model nitrogenase (Figure 8).^{15,25} In general, the introduction of Lewis acidic fragments into metal coordination spheres has great potential for new reactivity modes, akin to second coordination sphere effects highlighted by Shannon Stahl.

Connie Lu: I also believe that new reactivity will emerge from juxtaposing a Lewis acidic main-group metal with a transition metal. Theo Agapie's work wonderfully demonstrates how the redox potentials of a trimanganese oxide cluster, $\text{Mn}_3\text{O}_4\text{M}$

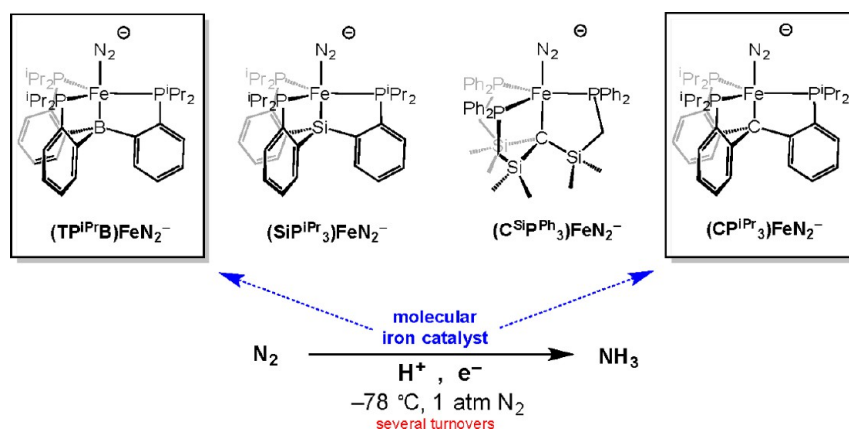
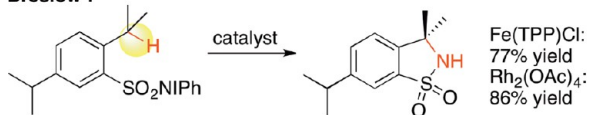


Figure 8.

(see Figure 9, bottom), can be tuned by simply changing the Lewis acidity of a redox-inactive metal, M. My group is also pursuing a similar strategy to directly tune the metal's electronic properties. I believe there will be exciting consequences on the metal's reactivity in the near future.²⁶

Christina White: François, I'm going to circle back to transition metals. I was really impressed by the work that was done recently from the Arnold group, where she "hijacked" a cytochrome P450 and got it to do organometallic chemistry, including cyclopropanations involving carbenes.²⁷ This is reminiscent of the classic work by Breslow and Gellman where they took a P450 and showed for the first time that you can generate an iron nitrene and perform carbon hydrogen amination chemistry. They also showed in later work that this chemistry can be done with simple iron porphyrins as well as $\text{Rh}_2(\text{OAc})_4$.²⁸ Interestingly, researchers chose to go on to fully explore and develop the $\text{Rh}_2(\text{OAc})_4$ chemistry, and the iron nitrene chemistry remained relatively unexplored. We were certainly inspired by this work in our own group, where we discovered an iron phthalocyanine catalyst that effects allylic carbon hydrogen bond aminations that are highly orthogonal to the allylic aminations we have done with palladium or those that have been done with rhodium nitrenes (see Figure 10).²⁹ For example, rhodium nitrenes

Breslow :



White:

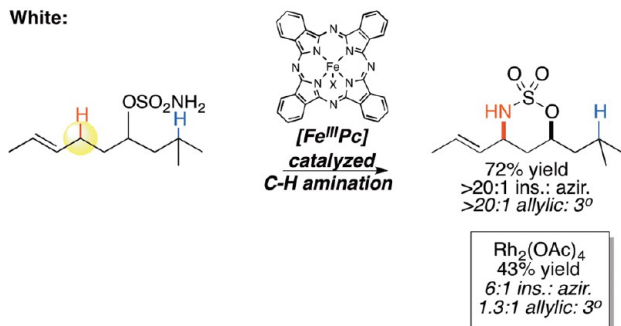


Figure 10.

generally give aziridinations and have no preference between allylic and tertiary (3°) carbon hydrogen bonds, whereas with iron nitrenes we see exclusively allylic C–H amination. This suggests that there are opportunities to realize new chemistries when second- and third-row metals are replaced by first-row metals.

Marina Petrukhina: I would like to bridge between main group and transition metals, as we do both. I've noticed a trend toward "dual catalyst" systems with two distinct metals, each with (in principle) a separate function. These can be either transition-metal or main-group species, and the sites can be independent or operate in a synergistic manner. The latter is more interesting, but remains more of an art at this point because the nature of the synergism is generally not well understood. But this makes it a very open area for research, computational studies, and applications as well. I think this is a very promising field, and there are increasing numbers of groups involved.

Christina White: An interesting paper that came out along those lines is by Schrock and Goldman, which reported a

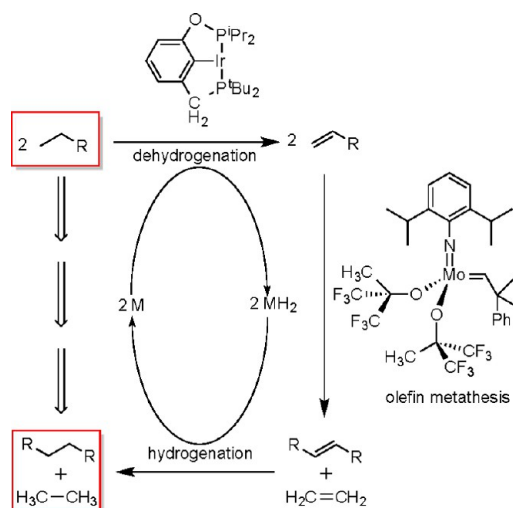


Figure 11.

formal overall alkane metathesis (see Figure 11).³⁰ They accomplished this transformation using two metals, Goldman's iridium catalyst that performs dehydrogenation/hydrogenation chemistry and Schrock's molybdenum catalyst that performs olefin metathesis. Such tandem catalysis where two metals are coordinated to work together in a catalytic cycle is not trivial to achieve, and this was a significant breakthrough.

Karen Goldberg: I agree. That was a wonderful paper. Building on previous alkane metathesis results, they were able to take alkyl arenes and long-chain alkanes and make linear alkyl arenes that can be elaborated to surfactants and detergents and other valuable commodities.

Edwin Webster: This goes back to the roots of the bioinorganic chemistry, where multiple active sites are coupled together to perform tandem transformations, for example, using both a calcium ion and a transition-metal ion, where the calcium ion serves as a Lewis acid and the transition-metal ion serves as a reactive or redox center. Taking steps from nature where the bioinorganic chemists have really made great strides—making the biomimetic complexes perform just like the natural systems, the difficult challenge is to learn the "best practices" to use the first and second coordination shells to tune the electronic and steric properties of the active center.

Greg Whiteker: A paper that I really liked was by Maurice Brookhart and involved converting 1-hexene from ethylene trimerization to *p*-xylene (see Figure 12).³¹ This is beautiful

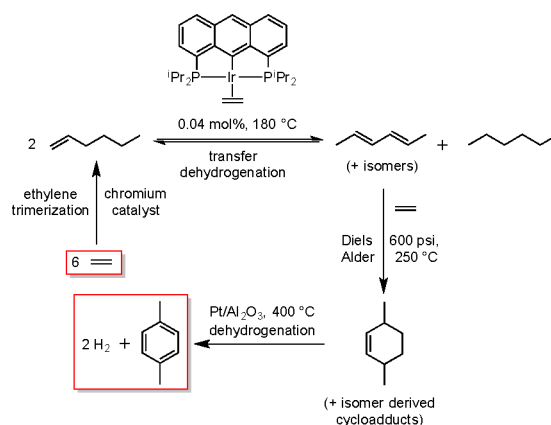


Figure 12.

chemistry, and as we will eventually have to wean ourselves away from petrochemical feedstocks, we're going to have to design replacements for current molecules or develop new routes to current molecules. *p*-Xylene is a precursor to terephthalic acid, an important industrial feedstock used on enormous scales. Hence, this paper may one day be a real landmark.

François Gabbai: There has been some very nice structural evidence for alkane complexes of transition metals, in particular the work of Andy Weller,³² who managed to reduce an alkene directly coordinated to rhodium, obtaining in this manner an alkane complex (see Figure 13, top). Jeff Long has also been

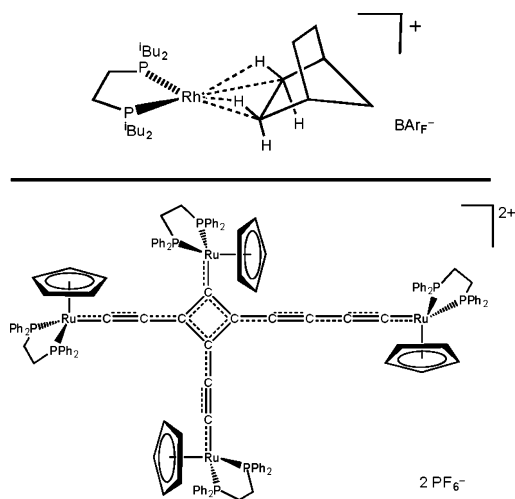


Figure 13.

able to structurally characterize small alkanes coordinated to unsaturated iron(II) center within the interior cavities of a MOF.³³

Robin Bedford: The synthetic methodology that Andy Weller employed to isolate his σ -alkane complex—a solid-state reaction but with the alkane introduced via the vapor phase³²—was really neat.

Tong Ren: There has been a lot of discussion of catalysis, but another important aspect of organometallic chemistry involves materials. For example, there have been many groups working on OLED or photovoltaic materials. However, the specific case I want to bring up is much more fundamental research. Recently, *C&EN* highlighted the work by Lapinte and Bruce,³⁴ where two Ru-capped octatetraynediyl chains undergo a regioselective [2 + 2] addition to form a tetrametallic compound linked by a cyclobutene ring (see Figure 13, bottom). This rare compound represents a new topology for carbon-rich chemistry, which is distinguished from trendy graphite/graphene materials that are based on hexagonal geometries. Better understanding of the mechanism for such a [2 + 2] addition reaction may lead to the synthesis of new carbon-rich electronic materials.

Robin Bedford: Another recent *Science* paper that really stands out for me in the catalysis arena is from Chirik's group. It showcases the approach of replacing platinum-group metal catalysts by earth-abundant metal analogues, specifically showing that Karstedt's platinum-based catalyst can be replaced with a simple iron catalyst for hydrosilylations of industrially relevant substrates (see Figure 14).³⁵ The iron catalyst's activity is at least that of the classical platinum species. While this study does not feature a groundbreaking transformation, it does represent one of the first genuine examples where an earth-abundant metal catalyst looks like it has a realistic chance of replacing a platinum-group catalyst in a large-scale commercial homogeneous process.

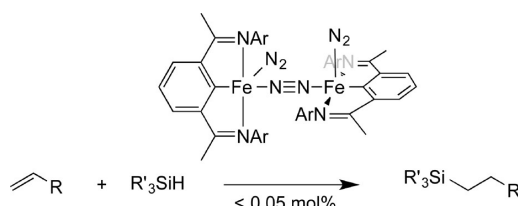


Figure 14.

Jack Norton: I certainly concur with Tong regarding materials chemistry and opportunities for organometallic chemists. In the case of OLEDs, there are challenges in engineering air stability, fine-tuning structures to achieve the right emission colors, etc.

Organometallics: We've treated both the present and the past. Let's now consider the major future challenges that organometallic chemists should be trying to address in the next few years. What societal needs and fundamental questions deserve particular attention? Where should we be heading, and why?

Michael Krische: Christina touched on this a little bit, but I'd like to emphasize that the merger of directed evolution and metal catalysis holds great promise. Catalyst loadings and selectivities in many metal-catalyzed reactions are modest. The tools of directed evolution allow one to select for enhanced efficiency. The power of directed evolution has been validated in the context of drug synthesis, as in Merck's route to Januvia (Sitagliptin).³⁶ Both Frances Arnold²⁷ and Manfred Reetz³⁷ have achieved impressive results, and it will be exciting to see where this goes.

Christina White: In our group, we have identified as a future goal the development of catalysts that will override substrate control for site-selective, intermolecular carbon hydrogen bond oxidations. This seems simple, but it is still one of the frontier problems, even in more established areas such as asymmetric catalysis. Our nonheme iron catalyst, Fe(PDP) (see Figure 15), selects for the most electron rich, sterically most accessible carbon-hydrogen bond within a complex molecule.^{38a,b} Qualitatively, we have identified the "selectivity rules" of this catalyst which rely upon the basic physical organic properties of an organic molecule: i.e., electronics, sterics, and stereoelectronics. This selectivity is largely dictated by the substrate: Fe(PDP) relies on the constructive combination of electronic (favors the most electron rich site), steric (favors unhindered site), and stereoelectronic (favors site where strain relief is possible) factors within a molecule to favor a single site of oxidation. However, what if one wants to oxidize an alternative site? The only option was enzymatic catalysis via a directed evolution approach that worked for one specific substrate. We asked ourselves: could a small molecule catalyst be developed that would shift site selectivity based on placing greater emphasis on one of the physical organic properties of a molecule? By doing so, the selectivity was also general (all molecules have these properties) and predictable. Excitingly, we recently discovered a simple small molecule catalyst [Fe(CF₃PDP)], that achieves high levels of catalyst controlled site-selectivity based on a design that renders catalyst/substrate interaction paramount while maintaining structural flexibility that enables generality in substrate scope.^{38c} A quantitative, predictive model was also developed that correlates the basic physical organic properties of a molecule to site selectivities as a function of the catalyst.^{38c} Ultimately, we envision a series of catalysts that would allow one to take a very complex natural product and oxidize different carbon-hydrogen sites with oxygen, nitrogen, and even carbon. Moreover, the quantitative model could be transformed into a user-friendly computer program where one simply inputs the molecule and the site of oxidation is predicted based on the catalyst. This would have an immense

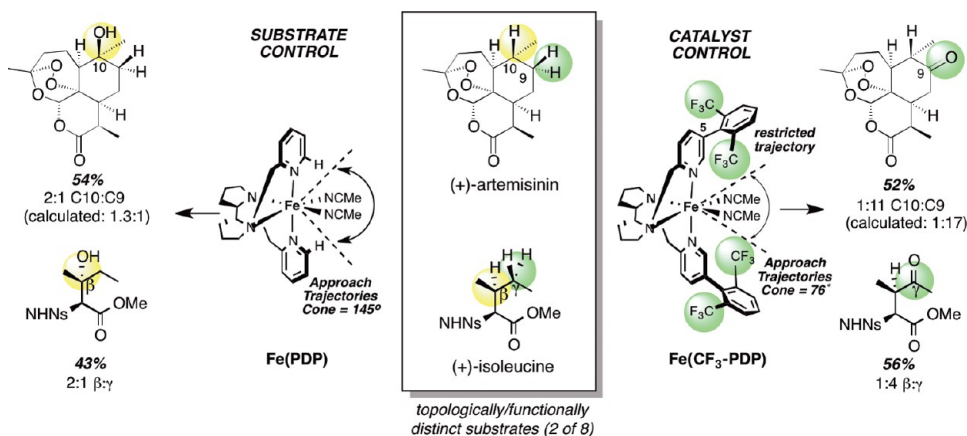


Figure 15.

impact upon drug discovery and development, and allied areas. Basically, it would render complex natural products as readily modifiable starting materials for drug discovery.

Don Tilley: In a related vein, it would be useful to develop arrays of catalysts that can operate in a cooperative manner, *via* appropriate regulatory mechanisms that allow turning the catalysts on and off.⁴⁰ These catalytic systems might model those found in biology. The development of regulatory mechanisms for synthetic catalysts is an interesting challenge for the future, as is the general approach of utilizing catalysts that work in concert. I think there are a lot of opportunities for multicatalytic systems, but we may need regulatory mechanisms for triggering and/or blocking catalyst activity, in the way that allosteric effects control enzyme function.

Jack Norton: Something I've said in meetings like this numerous times—I'll take advantage of the opportunity to say it again—is that researchers should seek to catalyze new and different reactions. Although there is a lot of lovely stuff done out there, often you see people competing to find better ways of catalyzing the same “fashionable” transformations. There are a lot of reactions of interest to the synthetic community that are not attracting a lot of interest from the catalytic community. There should be more attention paid to what's going on in organic synthesis to help identify new transformations that need to be addressed.

Organometallics: Can you suggest a reaction that deserves more attention?

Jack Norton: Bromination comes to mind, for example.

Makoto Fujita: Do you mean like methane to methyl bromide? Or do you mean like a steroid and an α -hydroxyl group at position seventeen? Or all of the above?



Prof. Makoto Fujita, The University of Tokyo.

Jack Norton: I'm thinking both of C–H bonds, and halogenation in general.

Patrick Holland: In terms of discovering new transformations, an interesting limitation of most catalysis is the need to go thermodynamically downhill. But if one finds a way to plug light energy into reactions, then that constraint can be relaxed. There are many reactions that are not on the radar screens of chemists because they're uphill without light energy. Unfortunately, there are a lot of challenges that need to be overcome. One has to understand the light absorption. One has to understand different spin states and how they interconvert. Most of all, one needs to understand the excited-state chemistry of reactive organometallic compounds a lot better than we do now. Nonetheless, I think there's a huge amount of potential for finding new reactions and transformations in this way.⁴¹

Don Tilley: If you look at the cost of solar electricity over recent years, it is dropping rapidly, and it is projected to continue dropping rapidly. As solar electricity becomes more available, it will be natural for chemists to start thinking more about reactions like that.

Patrick Holland: Along those lines, there's a lot of important work on light-mediated proton reduction and CO₂ reduction.^{42,43} These are certainly very important targets, but chemists should be looking at a broader range of transformations.

Jaqueline Kiplinger: In an endorsement of what Pat has said about photochemistry and Tong's comments earlier, in the area of actinide chemistry we are seeing some totally new reactivity patterns. Decades ago, Tobin Marks looked at the photochemistry of the heavy elements, but the field then remained dormant for many years. In the past few years, both my group and Steve Liddle's group have uncovered a number of unexpected photochemical transformations, including the syntheses of nitrides (see Figures 16 and 17).^{44,45}

Shannon Stahl: I have a preliminary and then a main comment.

First, our discussion involving light has overlooked recent breakthroughs in “photocatalysis”, or whatever equivalent term you want to apply. Thanks to Tehshik Yoon, Corey Stephenson, David MacMillan, and others, there is a whole collection of light-driven reactions initiated by single-electron or energy transfer, including reductions, oxidations, and redox-neutral transformations, that are transforming the way people think about synthetic chemistry.^{46–48}

Second, there has been a dramatic increase in the global supply of hydrocarbons in recent years and this is likely to continue. I have mixed feelings about this, as I worry that it will deemphasize the funding and attention given to solar energy conversion. Nevertheless, the last 6–8 years of focus on solar energy has reinvigorated the use of electrochemistry within our community, in a way that I did not perceive in the first 15–20 years of my scientific career. There's a whole new generation of people that are now using

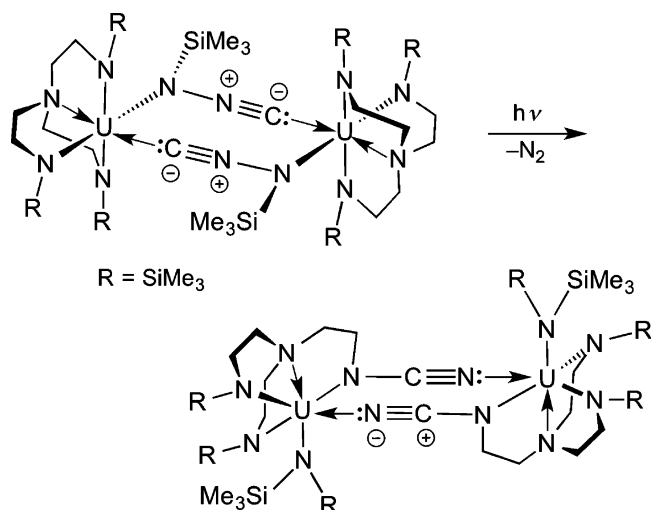


Figure 16.

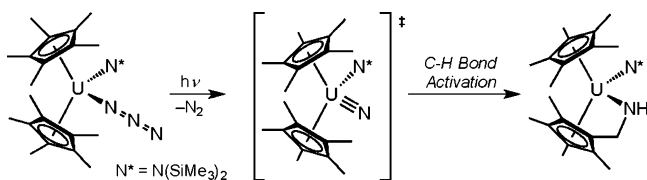


Figure 17.

electrochemistry as a result of the attention on solar energy conversion, and I think we're going to see a lot more of it, ranging from light-driven photocatalysis mentioned earlier to electrochemical synthesis and catalysis. We're going to see it throughout the literature in the next 5–10 years. It is not a new technique, but this "rediscovery" means that many people will be using it that would not have otherwise used it.

Janis Louie: I'm going to switch gears and go to an open field where organometallic chemists could have a large impact, but have not done much to date. It is perhaps the flip side of Karen's comments regarding methane and methanol. Here one is trying to take what is often a waste product (flaring) and turn it into something useful and transportable. This concept should be expanded to all hydrocarbons, and I'm especially thinking of waste polymers. There is some work now being done on the catalytic degradation of cellulose and related materials. In general, we work on the premise that the use of pure starting materials leads to the best products. It is what we teach our students. But, what about developing catalysts that are selective despite the purity of the starting material? This type of selectivity and bond activation could allow degradation of waste polymers without necessitating waste separation. We could find inspiration from work done in the bio-organic field where one bond is activated selectively in the presence of numerous functional groups.

Jaqueline Kiplinger: Lanthanides factor critically into so many materials, and we have a challenge regarding China and their control of the rare-earth market. I wholeheartedly endorse the concept of engineering better rare-earth catalysts, but I also feel that it is prudent to develop replacement catalysts for processes that already involve rare earths. This will lessen the chances of being held captive due to a sudden change in availability.

François Gabbai: In the context of future challenges, energy harvesting and storage is clearly a big one. We have seen the rise of organic photovoltaic materials, and I would predict or



Prof. Janis Louie, The University of Utah.

would like to see an increased use of main-group elements in such materials. One of the key ideas is that the incorporation of electron-rich or -deficient main-group elements in such materials can be utilized to tune their electronic properties. We have already seen some elegant efforts with elements such as boron and phosphorus and I would predict that this field will continue to grow.

Karen Goldberg: I want to return to Janis' comments about using waste products and biomass. There have been quite a few articles in the last couple of years in which organometallic catalysts are used to transform biomass. This is an area that has not received a lot of attention by organometallic chemists until now. Normally we think of trying to use organometallics to activate very unreactive C–H bonds in hydrocarbons. In contrast, biomass has lots of functionality already in it, so there's plenty for the metals to chew on. But you have to be able to cleave the bonds selectively. The goal here is to convert the biomass to valuable molecules that are smaller and less functionalized.

Also in terms of using waste materials, we need to consider whether the catalysts we are creating will work in the presence of the impurities contained in the waste. You often lose the advantage of using a *waste* material if you have to purify it. For example, some scientists giving talks on glycerol claim "it's basically free because it's a waste product from biodiesel production". It turns out it is not actually free unless you can use the *waste* glycerol without purification. We did some work in our lab where we got some glycerol from a local middle school teacher who makes his own biodiesel in his garage. It was fun to actually use real crude material that had all the extras in terms of impurities and to see how our catalyst responded. Gratingly, we got our catalyst to work.⁴⁹

Jack Norton: Although I'm for biomass utilization, it was already in favor around 1976–1980;⁵⁰ it is not that new, understandably, and inevitably and perfectly reasonable things come into fashion and go out of fashion.



Prof. Jack Norton, Columbia University.

Karen Goldberg: This leads into the old joke about why it is called RE-search.

Shannon Stahl: I'd like to touch upon another old theme that is being rediscovered: base metal catalysis. There's Ullmann coupling, the work of Jay Kochi, and lots of established industrial catalysis that uses first-row transition metals. But, in terms of fundamental research and opportunities to discover new reactivity, there's a lot here. And I think the question is what kinds of new mechanisms, what kinds of new transformations, even with similar substrates, might you access using first-row metals? I think this is clearly going to be a major theme in our field over the next 10 years. This topic probably feeds into the next question.

Organometallics: Green chemistry continues to expand as a discipline, and the ACS has recently launched a new journal that covers this field. Do you see this as an area of opportunity for organometallic chemists? Do organometallic chemists need to be more cognizant of the principles of green chemistry in their own research?

Jack Norton: I can start with that. I just refereed a paper for the journal *Green Chemistry*, and it was one of the worst papers I ever saw in my life. There is a certain level of piling on this particular bandwagon in the interest of not terribly good science. Some of this is inevitable in any popular field, but I judge there to be more in green chemistry.

Jaqueline Kiplinger: We all strive toward making materials in better yields using less toxic chemicals, if possible. I think as a community we came quite far as green chemists before green chemistry became fashionable over the last few decades. With an eye toward safety, solvent stills are gradually disappearing, and all of the waste that goes with them. In general organometallic chemists were ahead of the green chemistry field, we just did not call it green chemistry.

Christina White: I see many opportunities because, as pointed out numerous times during this discussion, nature has mastered so many transformations that chemists have not, like methane to methanol, using the most abundant, nontoxic metals possible, such as iron and copper. Thus, there is an absolutely tremendous opportunity not just to mimic some of the second- and third-row transition metals but also to discover orthogonal reactivities that some of these traditionally used metals really cannot do.

Some of the points that Jack brought up are really important. If a first-row metal is being applied to cross-coupling chemistry, I think the efficiency and scope has to be very good before the process is adopted in industry. Just using a first-row metal is a good step forward, and if you can show some interesting reactivity, that is great. However, any new process ultimately has to meet the same very high bar set by established processes.

In an extension of what Jackie said, I view organometallic chemists as ahead of the curve on green chemistry because by developing fundamentally new reactions and bond disconnections that allow organic chemists to put molecules together in very dramatically different and streamlined ways, one cuts out steps and makes syntheses more efficient. As Jack pointed out, researchers do not necessarily point these things out explicitly.

Connie Lu: A great area of opportunity for organometallic chemists is to move into water as a solvent. From a practical standpoint, water is an ideal solvent, but most homogeneous catalysts are not compatible with water. If we can make organometallic compounds that can function under air and in water, then we would be able to apply their use more broadly.



Prof. M. Christina White, University of Illinois at Urbana-Champaign.

Karen Goldberg: The risk in water is that you wind up at the end of the reaction with contaminated water that then has to be treated. This highlights some complexities in green chemistry and sustainability. When people do a green chemistry analysis and a life cycle analysis, they do not always come out with the same result. In any case, wastewater treatment introduces additional expense and issues that can mitigate the advantages of water as a solvent.

Shannon Stahl: I agree with both the desirability and problems associated with aqueous solvents. When the focus is on biomass, we are clearly finding that we just do not have the catalysts that can operate in the way we want them to. I completely agree with Karen's point about life cycle analysis, and the problem is that many of us academics are not really equipped to deal with this issue effectively. On a separate note, I'd like to give a "shout out" to pharmaceutical companies. I must admit—and this is just my own personal experience—that I was very turned off by the term *green chemistry* early in my academic career, as it was a buzzword that often seemed to be used to justify bad science. What pharma has done in putting out target "green" transformations, forging relationships with academics, and sponsoring precompetitive collaborations, is helping to rescue the term. Dow and other companies are also on board here. I give kudos to the industrial folks that are helping to reshape and reinvent the term green chemistry away from what it became in the early years.



Prof. Shannon Stahl (left), University of Wisconsin-Madison.

Greg Whiteker: From my vantage point at Dow, green chemistry from a process chemistry perspective is really nothing new. If you look at the principles of green chemistry, they are completely aligned with what we try to do in developing chemical processes. Every pound of material that we put into a chemical process that does not leave as product is waste. It is not something that I was taught as a graduate student, but I think

having a holistic view of an entire process to make a complicated organic molecule is really required. Too often one fixates on a specific transformation in a sequence, and I'm guilty of that having done a lot of hydroformylation chemistry. At the end of the day, everything has to work together to make a sustainable process that minimizes waste and impact on the environment.

Makoto Fujita: I agree that organometallic chemists have been doing green chemistry before the emergence of green chemistry. But I sometimes feel that green chemistry is much too conceptual. With any new field, there is the scientifically or "nuts and bolts" new, and the conceptually new. For example, the discovery of the metal–carbon bond can be viewed as the "ground zero" of organometallic chemistry. In contrast, I cannot find any new discovery at the beginning of the green chemistry. I agree that this is an important field, not just for organometallic chemists but for all chemists. But it is so conceptual, it seems to cover everything; fuzzy boundaries and ground rules can lead fuzzy minds to do fuzzy science.

Tong Ren: In this regard, I consider there to be an important difference between what is called green chemistry and what is called sustainable chemistry. The latter suffers less from the problems that Shannon describes.

Michael Krische: In my view, green chemistry becomes most evident where one finds the greatest economic selective pressure. For example, the efficiencies achieved in the largest volume applications of metal catalysts are uniformly outstanding, whereas those observed in pharmaceutical synthesis are uneven, as a less-than-perfect step may not impact profitability as much due to the high-cost clinical trials. I think there are a lot of misconceptions regarding green chemistry, and I agree with Shannon the involvement of process chemists have raised the integrity of this area.

For example, we've talked a lot about CO₂, which is a truly inexpensive building block, yet CO₂ activation is often accompanied by the stoichiometric use of ultraexpensive reagents. If one is going to activate something cheap, one has to use something cheap. One has to consider the degree of separation between the reagent and the feedstock. I'd love to see an efficient Fischer–Tropsch type process involving CO₂ based on reverse water-gas shift reactions.



Prof. Michael Krische, The University of Texas at Austin.

Marina Petrukhina: I agree with Tong that sustainability is a much better term than green, and as Jackie noted, we all started thinking in these terms a long time ago. Saving on any material, producing less waste, and using more reasonably priced starting materials, have been in the forefront of reaction design since our grandparents were chemists. Whenever one carries out any transformation, be it exploratory chemistry or a known process,

one thinks about the costs involved, waste production, the energy cost, the whole nine yards. That falls under the sustainability theme, but it is not a separate area. It is just an overarching conceptual term as Makoto mentioned.

Jaqueline Kiplinger: As Rich Eisenberg has said before, "It's Not Easy Being Green."⁵¹

Organometallics: Many in the synthetic chemistry community believe that journals should be able to provide more reproducible experimental procedures. What in your opinion are some of the obstacles and problems in this regard? Even with *Organic Synthesis*, 12% of the submitted procedures are typically found to be irreproducible.

Robin Bedford: I have some views on this one. I'm going to start off by saying as synthetic chemists we really should not beat ourselves up too much. Have you tried reproducing materials publications? There are some pretty esteemed journals out there, and when you start trying to reproduce the reported materials stuff, it seems you need to assume it is not going to work. Anyway, back to organometallic, organic, and inorganic synthesis. One of the issues in the area that I work involves catalysis where impurities in the system turn out to be responsible for the chemistry. This has led to a number of retractions, or follow-up publications that show an impurity is responsible, which apparently does not necessitate a correction or a retraction of the original article. One thing that might prove helpful in better journals, particularly ACS journals, is to require a checklist for new catalytic processes. It certainly would be prudent with commercially available materials—be they additives or ligands or whatever—to use and cite more than one vendor source, and make sure that the chemistry is reproducible when the supplier is changed. This would have prevented a lot of these retractions. The checklists could be formalized, akin to those used by many journals for compound characterization and purity.

Marina Petrukhina: There are a lot of issues involved in the reproducibility of preparative procedures, and the purity of starting materials is certainly one of them. You buy a starting material from one company and it works, and buy the same starting material from another and it does not. However, the cost should not be put on investigators. We're getting pennies for fundamental research, and the bigger issue is the company, which should somehow be responsible for the materials. I do not know how to make them responsible, but I do not feel like we have to check and test their products as a free service.

Robin Bedford: The issue is that if you buy, for instance, potassium fluoride from different suppliers, you'll have different impurities. The samples could all be 99% pure, but just having that level of purity is not good enough. One needs to know what the trace contaminants are, and also from batch to batch of a given supplier.

Marina Petrukhina: Most authors report suppliers in their publications.

Robin Bedford: Yes, but they usually report only one set of suppliers. In my field, it has been the case recently that one batch of a material from one supplier is at fault. It passes inspection by sight and all screening criteria, but there is some impurity in that batch that gives rise to false positives. The only way one can get around that in the short term is by using different suppliers for each component of a new process, particularly those where one is throwing in a lot of different additives to make the reaction go. These are particularly prone to the witches' brew scenario.

Michael Krische: Does not the ACS forbid authors to mention the vendors?

Organometallics: This part of our Author Guidelines is based upon longstanding policies at *J. Org. Chem.* and *Org. Lett.* and a number of other ACS journals. Basically, it is discouraged to specify instrumentation vendors and suppliers of routine chemicals unless there is a specific justification. Initially, these policies were in part a reaction to lengthy “general” sections of experimental sections that turned the first few paragraphs into the equivalent of a television commercial or newspaper advertisement; is a glovebox manufacturer relevant? In some of my own papers, I specify vendors for all highly fluorinated materials used, as there are availability issues. In other papers, I refer readers to a doctoral dissertation where the student has spelled all of this out. Back to *Organometallics*, we are flexible if authors wish to provide an exhaustive list of vendors in the Supporting Information (SI). But overall, there is no consistent ACS policy. *Organometallics* can set whatever policy best serves its readers and authors, which is one reason why we are talking about this and also why this (as a result of this Roundtable) will be a topic of discussion at our upcoming Advisory Board meeting next August.

Jack Norton: Rather few authors include vendor information nowadays because they are under the impression that the policy at least discourages it.

Karen Goldberg: I talked about this question with my students, and they came up with what I view as some very reasonable ideas. One was that instead of reporting the best yield for a synthesis, a range of yields should be given. This would serve as a check that the experiment had been done more than once. They were also enthusiastic about including all spectra in the SI. Thus, if one observes a small impurity when synthesizing the compound oneself, one can see if the same impurity was present in the samples prepared by the original researchers. Although microanalyses are good indicators of purity, my co-workers voiced the suspicion that a researcher might have tried ten recrystallizations to get one sample that passed. Now that all spectra are digital, I do not see why they cannot all be routinely incorporated into the Supporting Information of publications.



Prof. Karen Goldberg, University of Washington.

Edwin Webster: Current journal policy states that if the elemental analysis of a compound is not acceptable then “authors can...supply copies of NMR spectra...that establish the absence of detectable contaminants”. Would such a process of including all spectra in the SI require having all the spectra correctly assigned? Should it be a rigid requirement for every

compound (with assignments), or just a requirement if you were able to collect the spectra?

Karen Goldberg: Right now the most common format involves a list of chemical shifts, associated multiplicities and *J* values, and finally assignments. It would also be useful to have the full spectra where any impurities could be noted.

Janis Louie: This is a good idea, but it opens up the door for the reviewers to say, “oh, you can’t isolate your title compounds in pure form”, even if the offending peak is very small. However, the paper could be a valuable contribution nonetheless.

François Gabbai: Whatever the purity is—regardless of the criterion, which could be ultrasensitive—it should be disclosed.

Janis Louie: It should absolutely be disclosed, but consider the scenario where after multiple tries “I got my one batch that passes and I’ll show spectra from this one”. Is this acceptable?

Robin Bedford: I note that in organic methodological chemistry, yield is sort of king, but in organometallics yield is not king. If one reports a 50% yield, then it is 50% yield. Colleagues do not complain about that.

François Gabbai: As an Editor, I believe the level of purity should be openly disclosed by the most appropriate means. I have no trouble when an author communicates along the lines of “we made this compound and based upon NMR it’s 85% clean”. The referee can then decide if this is sufficient for the science reported, and whether the science is important and of high quality. It is all a matter of transparency. There is a perception that a new compound is unpublishable when it does not pass microanalysis, but this is simply not the case (and there are good reasons why certain types of compounds do not usually pass microanalysis).

Don Tilley: We’ve probably all experienced cases when one co-worker could not reproduce the results of another co-worker. I find that this often traces back to some level of detail, observation, or manipulation that was not obvious to the first person and therefore was not recorded in detail. I speak with everyone who comes into the group and try to impress upon them the importance of writing down everything, even if it seems trivial or unimportant at the time. To reinforce this point, I provide a few anecdotes. However, I think it would be better if there were a published resource that addressed this issue in a detailed and convincing way, perhaps using anecdotal evidence but bringing the point home in a larger context. There are publications that come out occasionally on things like this—on ethics and science or some related issue.



Prof. Don Tilley, University of California, Berkeley.

Patrick Holland: I would like to build on what Don has said. I think that doing notebook checks is important. We have all had times when we look at a co-worker’s notebook and they have written only the starting materials and products. I guess

they think they are going to remember what they did without notes, which sounds crazy to me because it is unlikely to work reliably. It comes down to good notebook skills: when someone does not keep a good notebook, inaccuracies sneak in and constitute one source of irreproducibility.

Robin Bedford: I want to come back to Karen's point about quoting a range of yields. I am not so comfortable with that. In catalysis there is often an element of experience and getting up to speed, and then one gets reproducibly high yields. So does one include the 75% obtained the first time, or only the 97–99% that one got the final three times? Any cutoff point is always arbitrary.

There is another issue, and that it is not just the students and their notebooks; we advisors are slightly guilty as well. We started publishing in the days when there were good, solid experimental sections at the ends of the papers, but now many experimentals are reported in the SI, and we are not using this resource perhaps as well as we could. It is now possible to write much more extensive experimental sections, and to include photographs and even audio or video. If we were a little bit more creative and energetic, this could provide other avenues for bettering reproducibility. Certain authors often publish an exquisite level of detail in very extensive SI sections. Steve Buchwald would be one example. One often finds in his papers lots of details and observations on precisely what happened. In any case, we as the primary authors have to involve ourselves in this crisis. It is not just a case of relying on co-workers and their notebooks and memories. Much is lost in the cookie-cutter compression into the standardized language of the experimental section.

Lastly, on the topic of SI, another group of people who are central to this issue are the reviewers. I fear that some reviewers of full papers come to the conclusion that everything looks nice in the main manuscript, and do not find the motivation to go line by line through 50 pages of SI. Editors really need to make sure that as a community, reviewers are putting as much emphasis on the information in the SI as in the main text itself.

Makoto Fujita: Although some organometallic reactions may be difficult to reproduce, there is a much more serious problem in biology. That is one reason why Nature Publishing Group established two journals, *Nature Methods* and *Nature Protocols*. For submissions in which the experimental work is clearly demanding, the Editor invites the author to submit the protocol paper as a separate manuscript. This is an excellent idea that underscores the importance of giving serious attention to written procedures. It undoubtedly decreases the frequency of reproducibility problems.

Jack Norton: I want to endorse what Pat said. It is extremely important to do notebook checks on students, and that ought to be a part of our responsibility as research group directors. I do it once a year. I'm not saying I should not do it more often, but it is important to do it at least that often.

Patrick Holland: This is one of the key ways in which we train our graduate students to be effective and accurate scientists. I sometimes wonder if professors think their students come in knowing all about notebooks from their sophomore organic chemistry lab course. This is rarely the case, and this is why we need to help them.

François Gabbai: In my group, I now ask that all laboratory notebooks be presented at both the preliminary exam and final



Prof. Patrick Holland, Yale University.

defense. That is roughly 2 years and 4 years into doctoral research. This has certainly improved the quality of notebooks in my group.

Greg Whiteker: I would like to encourage the adoption of electronic laboratory notebooks (ELN). My department at Dow switched to an ELN about five years ago, and this has enabled everyone to keep better notebooks, myself included. It is very easy now that all of our spectroscopic, mass spectrometric, and related data come in electronic form. It is very easy to append things as PDF files or directly put FIDs into the notebook. They are searchable by structure, and make it very easy to look at what your colleagues are doing. There is more impetus for individuals to keep a timely, accurate notebook because Jack is less likely to limit himself to an annual inspection. It is simple, and perhaps even more effective, to do checks more frequently.

Janis Louie: Are there shareware electronic notebooks out there or are these all high-price customized programs?

Greg Whiteker: We use Cambridge software that is in the ChemDraw family.

Marina Petrukhina: I'm a big fan of such protocols as this is a very good practice. My group uses electronic reports, and it is very easy for an advisor to make comments and request that certain things be brought up to standards. We do not use any special software, only a shared drive where the students file them and everyone can access them.

Don Tilley: Another potential tool that could address experimental reproducibility would be questions listed in the form that all reviewers receive when they referee a manuscript. It might be useful to ask point blank "have you read the experimental section?" or "have you checked the chemical shifts and coupling constants in the NMR spectra?" or "do the experimentals for the syntheses of new compounds give researchers a clear idea of how to repeat the procedures?"

Organometallics: Starting in 2013, *Organometallics* does not allow the experimental sections of full papers to be presented in the Supporting Information any more. This follows a policy pioneered by *J. Org. Chem.* There are some reviewers who simply do not give the same level of attention to the SI as the main text. With *J. Org. Chem.*, they basically only allow the presentation of spectra. However, our Author Guidelines allow for clearly subordinate information, such as the preparation of isotopically labeled compounds by methods analogous to those reported for unlabeled compounds, or characterization data for tables of known Heck coupling products or other series of compounds that have already been reported many times in the literature.

François Gabbai: One aspect of Don's point is whether reviewers should be directly asked whether melting points are reported, whether elemental analyses are reported, and so on. Is there sufficient proof of purity or bulk purity for each new compound? *Organometallics* could elaborate its questionnaire form in a number of directions.

Marina Petrukhina: *J. Org. Chem.* has a much more elaborate form, as well as a checklist for authors regarding compound characterization.

François Gabbai: An alternative is to ask the referee regarding the points that are covered in the *J. Org. Chem.* author checklist.

Robin Bedford: To help increase my co-worker's confidence that they are doing reproducible chemistry, we have established a sort of "I'll scratch your back, you'll scratch mine" process where, before something is submitted for publication, another co-worker in the group who is not necessarily an author repeats the chemistry. This gives one that extra little bit of security. Admittedly, it does not eliminate systematic errors within the lab, but it does eliminate systematic errors between co-workers.

François Gabbai: The ultimate extreme would be for the journal to have checkers as with *Organic Synthesis* and *Inorganic Synthesis*. There are many obvious reasons why this is not practical. But Robin's method is essentially doing this within one's group. Anything more would push authors to another journal. Editors have to strike a balance.

Robin Bedford: It worries me if a journal has an attitude of not wanting to chase authors away to other journals. I would want to have my papers associated with journals that are taking a strong stance on reproducibility. That is where our community should be publishing.

François Gabbai: I completely agree with you.

Connie Lu: The practice of having another co-worker reproduce data is a wonderful idea. The PI stands to benefit because if in the unfortunate circumstance that a co-worker is fabricating data, you can catch it before publication, rather than afterward.

Michael Krische: Would it be productive to have authors submit video tapes? Nearly every graduate student has a cell phone camera.

Organometallics: The journal is very open to photographic documentation and movies. These are underutilized. There have not been any videos uploaded in the last 4 years.

Jack Norton: Although this practice raises some issues, I personally ask my co-workers to review the Supporting Information of manuscripts I get to review. They do a great job.

Organometallics: The more eyes on any manuscript, the better. However, one should check with the Associate Editor handling the manuscript first, as confidentiality protocols have to be followed.

Organometallics: A recent Editorial by Amos Smith entitled "Data Integrity"⁵² stated that "research institutions...need to create an environment that fosters research integrity through education, training, and mentoring and by embracing incentives that deter irresponsible actions". What can be done to help maintain the highest standards in organometallic chemistry? What should research advisors, reviewers, and editors be doing?

Jaqueline Kiplinger: At some level it simply boils down to personal integrity, and you cannot prevent people from being dishonest. A lot of examples seem to be popping up now, so this is a hot topic. If people are going to Photoshop or liquid paper

in a not very obvious way, there's nothing you can do. Some are getting quite sophisticated in deception techniques, so to repeat, it is ultimately a personal integrity thing. If individuals get caught then they should be banned from publishing in that journal, and perhaps others. But at some level, you just cannot stop people from being dishonest.



Dr. Jacqueline Kiplinger, Los Alamos National Laboratory.

François Gabbai: What do you do within your group if you have a co-worker engaging in this type of behavior? And where do you draw the line?

Jaqueline Kiplinger: I had a postdoc who did not know how to keep a notebook, and I did not discover it until it was a little down the line and there was a question of whether that work was reproducible. I asked someone else to try to reproduce some experiments, and they could not. So we never published this work. If I were to catch someone in my group deliberately falsifying data, I would get rid of them.

François Gabbai: It is certainly true that some individuals have a natural tendency to engage in this type of behavior. However, I do believe we have a responsibility to educate, as some students may simply be unsure or naive as to what is right or wrong. One would hope that we all carry an appropriate value system within ourselves, but there are also choices that are not so clear. These are often highlighted in courses or textbooks on ethics.

Jaqueline Kiplinger: I naturally appreciate the educational and training component with co-workers. One sets a personal example and tries to reinforce ethical behavior. However, if you catch somebody blatantly doing something dishonest, you have to call them on it. Hopefully, this is in advance of publication.

François Gabbai: I agree with you.

Marina Petrukhina: We should start educating our graduate students as early as possible regarding these issues. A few years ago, my department started devoting the first seminar of each year to research ethics and integrity training. Several faculty members collaborate on designing the presentation to educate all incoming students, particularly those from other cultures where values may not be as entrenched or where lawyers have not stuck their noses into every aspect of daily lives. Anyway, I think something like this is a start.

Edwin Webster: Our department does the same thing, but added into an expanded first semester graduate course. The ethical training is tailored to things encountered by graduate students, including service as instructors. It is rich with case histories, and everyone is required to actively participate. Ethics training has also been incorporated into parts of our undergraduate curriculum.



Prof. Edwin Webster, The University of Memphis.

Robin Bedford: This type of training is really important. I do not believe we can do much about individuals who fabricate. It can be nearly impossible to spot someone who is dead set on just making data up, so things are going to make it through from time to time. But there is also a very large gray area, and as François emphasized, students may not always be aware of what is a borderline practice. Consider the example of impurities being surreptitiously removed from NMR spectra. However, solvent suppression software routines have been around for decades, and there are many accepted uses. But a co-worker may not realize that carrying out a solvent suppression routine and not adding an appropriate note to an experimental or a figure caption is essentially fabrication. We rely on the fact that good schools have good training and codes of practice, but this cannot be extrapolated everywhere. Perhaps publishers will be able to introduce online tools, and the plagiarism software that is being widely adopted is a step in this direction. I mean, now publishers have all of these statements of great, wordy text about what authors must and mustn't do, but they always look a little bit forbidding. An online tutorial tool with examples of what constitutes borderline or unacceptable behavior might actually be a very useful thing that could be introduced fairly easily.

Patrick Holland: There are a lot of gray areas that fall short of falsification where there is no current guidance from publishers. For example, how small does a peak have to be before you are not obligated to include it in a NMR peaklist? I suggest that *Organometallics* publish a list of discussion questions that one could use within research groups to clarify proper practices. This would help us get these points across to our students effectively.

Jaqueline Kiplinger: Perhaps journal submission guidelines could be more explicit with examples of good practices in experimental sections. This could include examples of formats or styles that are no longer acceptable.

Organometallics: Things are being done along these lines. The ACS has created a task force involving journal Editors, NMR experts, and others to draft a "best practices" document for NMR. This document has been approved, and the guidelines should be released shortly.

Jack Norton: I have some case studies of unethical behavior dating from my experience as an editor. I would be happy to share them, to the extent that I can protect confidentiality. If several editors were to combine their experiences, one would have quite an interesting "short course".

Janis Louie: I have a specific concern. There are some compounds that you are simply going to get in a purity range of 85% or so, and never higher. It may be tough to put the data in a format that conforms to whatever "rules" are devised for pure compounds. For example, it could be burdensome or even

irrelevant to present a complete peaklist. I worry about making something black and white, where not all compound syntheses are black and white. Some compounds are just more difficult than others.

Karen Goldberg: In response to Jack's comment, I think it is important to share case histories from journals. Everything usually gets hushed and not talked about. Nobody really gets the full story on anything. An investigation takes place, but the resolution is suppressed or hard to locate. Getting these out in the open is really important.

Jack Norton: For years I have been giving talks to high school students about the scientific publication process. They love this kind of stuff. There's nothing they like more than hearing of adults that have behaved questionably.

Jaqueline Kiplinger: Karen is right. These things happen and then there's a flurry of activity. We are at an interesting crossroads, and should take ownership and seize the opportunity of using this as a means of improving our profession, instead of hush hushing or relying on blogs such as ChemBark. One consequence of the recent flurry of falsifications is that people are now more aware and looking for them. I think we should use this as a turning point.

Connie Lu: As principal investigators, we have tremendous influence over our students in ways that we may not appreciate. We know where the bar is set for publishing, and pushing some students doggedly may prompt them to alter their data. If for example, the purity of a compound still does not meet publication standards, it is important not just to express disappointment, but to also say something encouraging, like "hang in there, you can get it". Be positive so that the co-worker does not get desperate or frantic and make a bad decision that can negatively impact you as well.



Prof. Connie Lu, University of Minnesota.

Edwin Webster: Data integrity is obviously important. But there's also the ethical behavior of a PI. Or a PI might act unethically with the co-worker following suit. The student may think "Oh, that's okay. I learned it from my PI – they did it so I'll go do it."

François Gabbai: We have spoken about the possibility of publishing examples of misconduct, but this is problematic. One is dealing with people, there are often legal issues, and presenting these incidents in a sufficiently impersonal or redacted way may be difficult. I'm simply not sure how to go about this in a first class way.

Edwin Webster: One could take a pure material and then deliberately add an impurity and record the spectrum. One could then suppress the impurity peaks or otherwise manipulate them into the baseline. In this way, an artificial case study could be composed. Obviously this takes someone's effort, but legal issues would seem to be avoided.

Organometallics: One continues to read about accidents in academic research laboratories, and the well-publicized death of a researcher at UCLA involved an organometallic compound, *t*-BuLi. What are the implications for organometallic chemists? What could be improved in our approach to safety?

Jack Norton: I have strong feelings about this subject and it is an extremely controversial one at the moment in my institution. I will say two things. One is that faculty members do have some responsibility to ensure that practices in their research groups are safe. Second, all co-workers have to be involved in the process as well. They are after all the people whose safety we are interested in, and the whole process is going to work better to the extent that they have direct involvement.

Robin Bedford: My institution has a very strong stance on safety, way beyond the obvious, about no one working alone, always wearing appropriate safety gear, etc. The intellectual engagement of each worker with safe working practice is absolutely paramount. It is not just about form-filling; although paperwork plays a role, it does not protect one per se. Its about thinking about safety each time you undertake a process.

As our former head of the department, Tim Gallagher, always used to say, just because you know in theory how to cross a road, does not mean that you stop looking in both directions every time you do it. He tried to drum a similar message into each of us regarding safety. One has to think about how to minimize risk every time one undertakes an experiment. Like Jack said, the absolute key to all of this is engagement.

Connie Lu: Our department is fortunate to have partnered with Dow in a unique program to improve safety. Last year, the safety officers from nearly every research group visited Dow facilities to learn first-hand about safety practices in industry, which we all recognize as better developed than those in academia. The students returned with increased safety awareness. More importantly, they advocated and implemented many new safety practices that have greatly strengthened the safety culture within the department. For example, the students conduct periodic lab tours, launched a web site with helpful resources, and introduced a brief safety moment before every seminar.⁵³ Our departmental chair, Bill Tolman, Frank Bates, the chair of Chemical Engineering and Material Science, and William Banholzer, the former chief technical officer of Dow, were instrumental in creating this program, but it really gained momentum when the students took charge.

Karen Goldberg: I read about that in *C&EN* and thought that sounded terrific. Industrial standards for safety are way beyond what they are in academics, and we have so much to learn from industry in this regard. It would be great if we could find better ways to interface with industry; there are not enough good mechanisms to facilitate such interactions.

Jaqueline Kiplinger: National laboratories such as Los Alamos have a lot of safety rules and training protocols in place. We have hosted visiting student researchers, who are exposed to this culture, which is far more extreme than in academia. Then they go back and generally share this aspect of their experience—for example, how radioactive compounds or waste are handled at Los Alamos. This transfer of know-how is perhaps not as systematic as with the Dow/University of Minnesota program, but everything helps, and this is an important collateral benefit of the visiting researcher experience.

Greg Whiteker: I want to emphasize what others are saying about changing a departmental culture. As graduate students, we're all trained to be independent, to be experts at what we're doing. By stressing independence, one creates an implicit barrier to someone admitting "hey, I've never done a reaction with LiAlH₄ on a hundred gram scale". The proper mindset is of course "I've never handled this reagent, what should I know about this workup". But will the co-worker admit to his/her colleagues or advisor that he/she needs to have someone else take a look at something or give advice? I certainly did things as a graduate student that I would not be doing today, and oftentimes I did not want to admit that I was sort of clueless. The cultural shift in industry is that we have sets of questions and checklists that we are required to go through. These may involve a new type of reaction, a new reagent, a scale that one is going to exceed, etc., and trigger a series of reviews. These reviews do not have to be horribly time-consuming, but they help. One of the best things one can do to improve safety is simply to get a colleague to look at the procedure and say, "what's the worst thing that could happen?". We call these peer reviews, and do them routinely. It is the first line of defense against something really bad happening.



Dr. Greg Whiteker, Dow AgroSciences.

Jaqueline Kiplinger: The synthetic community at Los Alamos has implemented something similar during the past few years, called "Plan of the Week". The goal is to have a second pair of eyes look at a process. Is it being scaled up or is there anything dangerous about the process that has not been realized?

Greg Whiteker: That is a really good way to help one's colleagues. At the same time, I believe that safety has to be a condition of employment. And I do not know if that is necessarily true in every research group. Chemists should know that there are certain safety policies that they have to abide by.

Don Tilley: This is true in the University of California now. It is definitely a condition of employment or even just being part of a laboratory. The UCLA accident has had significant implications for how we do business in the UC system. Just to give an example, we write SOPs, Standard Operating Procedures, for every chemical that we use in the lab. My co-workers have spent a lot of time preparing these. We give them to the departmental safety office for approval. In some cases, one SOP can be applied to a class of compounds, but nevertheless we have written hundreds of them. This step is definitely changing the culture. Also, for our SOPs we include a statement saying that just reading the SOP does not empower anyone to do the experiments described. Permission to carry out the procedure requires that the person has been trained, and then observed carrying out the procedure, by a senior person in the group or the PI.

Marina Petrukhina: At our department we had extensive discussions between faculty and the Office of Environmental Health & Safety, and that really helped to get them involved more heavily in training of our graduate students. Just as an example, they provided costly lab coats having antflammable coating to graduate students involved in synthesis and working as TAs. This is a relatively simple measure that makes a big difference in safety.



Prof. Marina Petrukhina, University at Albany, State University of New York.

François Gabbai: One issue with safety in a chemistry department is that although all faculty members have a deep understanding of what is safe and unsafe in the laboratory, we are not vetted by any formal mechanism. Even if someone is a member of a safety committee, a court of law might decide that that individual has never been vetted in any way by an authority. I guess that is an open question for the Roundtable. Who has the authority to declare, “Marina, you are competent, and you can be in charge of safety in your department”?

Don Tilley: In the UC system, this is addressed with courses. We take mandatory online courses. It is also assumed that you forget what you have learned every 6 months, so you have to repeat them periodically.

François Gabbai: We do not have that. But perhaps it is coming.

Jack Norton: The City of New York does much the same thing. The courses and tests are not terribly effective in my opinion. But the City does try.

Janis Louie: Has anyone encountered a test that they regard as exceptionally good or online training that is truly informative?

Patrick Holland: I just went through the online safety training at Yale. I expected it to be legalese and impractical. But the training session asked questions that one had to think about—neither black nor white but in the gray area. I think they did a great job. I do not know whether their training system is available to share with other institutions.

Greg Whiteker: I’m curious whether any of the academic departments represented here have monthly safety meetings, because that is a common practice in industry. One of the most helpful things that comes out are simple discussions along the lines of “here’s an especially reactive substance” or “here’s how you safely handle chlorine gas”, which lots of people do not know how to do. One recent meeting dealt with “here’s how you use *tert*-butyllithium”. These involve special topics outside of the normal required training. Another agenda item is what we call “near misses”, which are lessons learned short of an actual incident. The idea is to make sure everybody knows and the misstep is not repeated.

Organometallics: In 2011, we discussed the advice we would give to co-workers beginning academic careers. For this

Roundtable, let’s discuss the preparation of co-workers for nonacademic careers, either in industry or as entrepreneurs. How can we be more effective, and how could academic and industrial chemists better work together?

Robin Bedford: We try to take advantage of every opportunity of getting industrial involvement in a Ph.D. project. Typically in the UK this would involve at least a 3 month placement in industry for the student. From a pragmatic viewpoint, sending a student to work for 3 months in one of the companies where they might have a chance for future employment can pay many dividends. They get a first-hand impression of what it is like to work in the sector, but perhaps more importantly they start building up a network of contacts. That might include the individuals who would review their job applications later on. The experience might also include informal advice on how to prepare for interviews. I believe that is probably the most valuable training that we provide to our students. We have a lot of formal courses relevant to non-academic careers as well, but I think this is what the students find most useful.

Makoto Fujita: Are you doing internships then?

Robin Bedford: If one has an industrially funded project in the UK, part of the deal is that the sponsor provides a three month placement for the student as a minimum.

Tong Ren: That is certainly an effective way of training. Do you have any rules about when the placements are scheduled? For example, this might be after passing a doctoral prelim.



Prof. Robin Bedford (right), University of Bristol.

Robin Bedford: The placement would normally occur about two-thirds of the way through the research phase of the doctoral program, so that the student has a sufficient body of results that it will make it worthwhile to go off site. This is not so late that it will be difficult to make the most effective use of the training that they’re going to pick up in industry.

Greg Whiteker: Dow has summer internship programs, but they are primarily directed at undergraduates. We have some students come in for part of the doctoral research, but the mechanisms here are informal and are commonly connected to relationships with the advisor. These experiences are clearly valuable, also for us. Oftentimes the graduate students have no concept of what an industrial career is going to be like, as all of their professional contact has been with academic chemists. I would encourage all academic chemists to try to find ways of establishing connections with colleagues in industry.

Organometallics: Do you have any criticisms of things that academicians do, things they often miss the boat on?

Greg Whiteker: No, I do not think so. It is a two way street because industry oftentimes has a real need for secrecy. So we’re not sharing with you what our real problems are. Regarding the applied aspects of your fundamental research, we may not



Prof. John Gladysz, Texas A&M University and Editor-in-Chief, *Organometallics*.

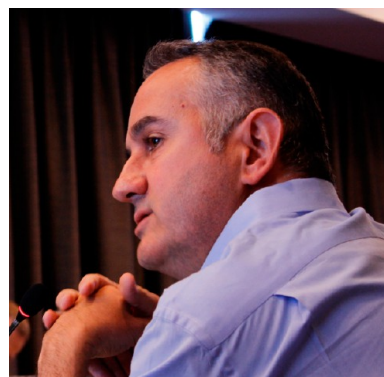
necessarily be able to share what is of particular interest to us. I believe one of the things that could really help students in their graduate work is to have some involvement with a multi-disciplinary aspect of their project. If someone is doing catalysis, interacting with a chemical engineering faculty member or having a joint project with someone in chemical engineering would be excellent preparation for an industrial career. One certainly learns in an industrial setting that no one discipline singularly contributes toward the new products and processes that industry is ultimately interested in. There is a wide variety of disciplines, all with complementary functions, that are involved.

Marina Petrukhina: I totally agree that this is a great way to educate students. In terms of internships, Europeans are way ahead of Americans. There are not that many internships offered by US companies. Greg, you mentioned something for undergraduate students, but I do not know of many domestic graduate internships, and this is a limitation. Fortunately, using my research connections with Siemens I have been able to send a couple of students to Germany, where there are good programs available. Students spend a few months in Germany learning not only chemistry but industrial culture, and that was a great career experience for them. One decided to go into industry after that and another decided against it, but my point is that the availability of US-based internships to bridge the graduate education/industrial connection is severely lacking.

Jaqueline Kiplinger: I want to echo what Greg and Marina have said. It is the same with national laboratories and the DOE complex. We have internships because we want to expose students to our culture, as many simply do not know what we do. Another opportunity, of course, is to do a postdoc at a national laboratory. I realize this sort of sounds like a plug, but this has really opened up some people's eyes as to whether or not they wanted to work in a certain area, and stay in our setting which is somewhat of a cross between industry and academia. There is a multidisciplinary aspect to most of what the national laboratories do, and this is another way of firming up one's interest with respect to a career in industry, a national lab, or academia.

François Gabbai: We have spoken about sending students to an internship in industry, but the reverse model is also quite effective. In other words, having representatives from industry come to our department for a day, an afternoon, or a few days. Under the right circumstances, someone from industry might find it advantageous to work in an academic laboratory for a period of time, and at Texas A&M we have recently had several such "embedded" scientists, courtesy of Dow and BASF. This has been a big help. These connections have allowed students

to realize that there is a world outside of the department, with great people and a different operating model. I want to ensure the chemical industry that this is a very effective mechanism for interfacing with students.



Prof. François Gabbai, Texas A&M University and Associate Editor, *Organometallics*.

Greg Whiteker: I cannot speak for other companies, but I'm not sure if there's anything in Dow's internship program that would prevent graduate students, say in their second or third year, from participating. Could it be that there's a mindset along the lines of, "if I'm gone for three months, that's three months of thesis research that I'm going to lose, delaying my graduation date". Is that a message they're getting implicitly?

Robin Bedford: We typically try to get some area of research going with the company that allows the students to take their new techniques from their research and produce data in an area that would broadly interest the company. This gets them something for their thesis and probably another publication as well. This addresses Greg's point about a delayed degree. With regard to François' point about hosting external industrial chemists, we've tried to do this for a long time. For example, Hans de Vries from DSM is a visiting professor at Bristol, and every other year he comes in and delivers a 2 day course on the industrial perspective on catalysis. This gets rave reviews from the students. Also, a few years back we set up a new means of educating some of our postgraduates. This involves sending them to 1–2 day industrial training workshops, which are getting more and more popular in the UK. These feature topical modules delivered by industrialists on subjects such as experimental design, intellectual property, and the like. Our students really engage with this.

Edwin Webster: Who pays for these things? We would love to have more interaction with industry, but the costs associated with these types of programs can be extensive.

Robin Bedford: The placement costs for the three month visits are met by the company as part of the collaborative contract they enter into. The training courses delivered in house are typically funded through recently established Centres for Doctoral Training. Funding for Ph.D. students in the UK has contracted overall, with much of the remaining cash being focused on these doctoral training centers, which have a strong skills training component. Institutions have to compete for these Centres, and part of the expectation is that the Centres should really engage with the end-user community to build and deliver graduate training that is relevant. For instance, at Bristol, we have the Bristol Chemical Synthesis Doctoral Training Centre.

Organometallics: Let's return to the future of organometallic chemistry. To what extent do you perceive limitations based upon instrumentation, infrastructure, or shared facilities? Do any new (instrumental) techniques hold particular promise for breakthroughs? What role is computational chemistry currently playing?

Don Tilley: Some of us have been involved in an NSF workshop on base metal catalysis yesterday, and I believe the theme of using more earth-abundant metals in organometallic chemistry is going to be a strong one going forward. This will mean some changes in the way we do research and characterize new compounds. Characterization tools have to be more broadly defined, and we need to bring in techniques that maybe have not been extensively employed in organometallic chemistry, to deal with odd-electron species and reactive intermediates. I see an evolution toward a toolbox that is more along the lines of what has been utilized in bioinorganic chemistry. A major challenge is then access to these more specialized techniques. Resonance Raman spectroscopy requires sophisticated instrumentation, and when local facilities for Mössbauer spectroscopy exist, they may cover some nuclei but not others. I believe we have to work together as a community to make sure that funding agencies recognize these issues and ensure ample opportunities for collaboration. Think of how useful a Web site-based directory might be. There are research groups that encourage interactions—Ed Solomon's comes to mind—but how does one, and in particular beginning professors, learn of the places that can host short-term visiting students, and their capabilities? There needs to be a funding mechanism to encourage collaboration—maybe a little money to the host research group, and/or a little money for the visiting student. There is a real need here that I perceive as a challenge for the field.

Robin Bedford: I wholeheartedly agree with Don. Some of us organometallic chemists are reasonably familiar with some of these techniques, but others are less familiar and struggle to try to learn how to use them. There's a lot of very good organic chemists out there doing first row metal chemistry. But they may not have any background in the specialist spectroscopic techniques needed to study paramagnetic intermediates, nor will they necessarily have access to the instrumentation, so it is really important that as a community, we make these sorts of collaborations available. In particular, I think that mechanistic studies that underpin first row metal chemistry are going to become increasingly important over the next few years.

Jack Norton: I have an emphatic comment about this panel question. My students increasingly investigate everything, and I mean everything, by NMR. It is hard to get them to do anything else, such as a melting point, IR spectrum, mass spectrum, etc. There are so many, often new, techniques that are overlooked. In addition to using new techniques, we need to remember to apply some of the classic old ones.

Robin Bedford: I guess you are talking about research involving diamagnetic compounds.

Patrick Holland: I can certainly empathize with many of these points, particularly as someone who is part of both the bioinorganic and organometallic communities. As Don implied, there are a number of techniques that have crossed over from bioinorganic chemistry into catalysis. For example, organometallic chemists are only recently using NMR widely for paramagnetic compounds, even though this is a longstanding practice in the bioinorganic chemistry community.⁵⁴

More generally, I think we can look at bioinorganic chemistry for the next wave of methodologies that are going to impact

organometallic chemistry. I believe that X-ray absorption and emission techniques are going to play important roles.⁵⁵ Magnetic circular dichroism is well-established in chemistry, but has a lot of promise in organometallic chemistry. Also, rapid freeze-quench has been applied to many bioinorganic systems, but has not seen much use within the organometallic community.

Makoto Fujita: Computational chemistry has been a major influence in chemistry and now pervades every aspect of the field. But in my opinion, this has now achieved equilibrium and is no longer a growth area. However, I wonder about high-throughput approaches to discovery in organometallic chemistry. This concept has spread into many areas, but I'm wondering where it will be truly useful. What is your opinion? Can we point to any successes?



Prof. Tong Ren, Purdue University.

Tong Ren: From what I know of recent advances in olefin polymerizations, Dow would seem to be a leader.

Greg Whiteker: I recently had a conversation with an academic chemist about their use of high-throughput techniques in identifying leads, and then following up with the more traditional physical organic kind of organometallic approach. I did not come away convinced that high-throughput procedures made for valuable training for graduate students. Unless one is designing new tools or methodologies, I'm not sure doing a lot of screening experiments really advances one's graduate education.

Tong Ren: Or helps to prepare you for what's to come?

Greg Whiteker: It could help to prepare you for going into an area where it is a useful tool. In that respect it would be valuable for training. To me, the real value of high throughput is the idea of doing things in parallel. The ability to generate buckets of data from an extensive series of mechanistic experiments or synthetic runs can be extremely useful.

Patrick Holland: It is useful if it helps one guess which catalyst will be optimal before undertaking a backbreaking mechanistic study.

Robin Bedford: I'd add a note of caution to high-throughput screening. We currently only do very low-throughput screening, but we have done a bit of high(ish) throughput in the past with iron catalysts. However, we completely overlooked some very simple systems because it turns out that the order of addition was hugely important. There are so many assumptions built into high-throughput chemistry, and you can miss some good stuff.

Greg Whiteker: Despite Makoto's comments, I would like to put in a plug for computational chemistry. With the availability of clusters to do DFT and ab initio level calculations, chemists no longer have to use things like PH₃ to model complicated

phosphorus ligands, and this has greatly increased the utility. One can actually do DFT calculations on the real systems. However, I'm a little concerned that just because we can input something on the computer does not mean that we really understand what we are doing. I would like to see the theoretical community play more of a role in trying to make sure that we're doing these things well.

Edwin Webster: The marriage between experiment and theory is very important, as is identifying the places where one can make a real intellectual contribution to a project. It is not just "can I calculate the structure of something I already have the X-ray crystal structure of", and one sees far too much of that now. It is easy to say, "let's chase an experiment" or "that was the experimental result, let's see if we can compute the same thing". This usually adds little to a paper (unless the computation gives some fundamental insight into how a process is occurring). What is important is to use computational chemistry to look for new things, new ligands, new reactions, explore reactivity, etc. Recognizing the appropriate time for the appropriate methodology is one thing that is very lacking in a lot of the literature in general. Too often it is thought "well I got this result, it must be meaningful" and it is not necessarily. And that is a big problem you see when reviewing papers. People who should know better and people who do not know better publish work and their description of the methodology, for instance, is just incorrect. It is listed or cited incorrectly in the paper (recognizing that everyone makes mistakes). Sometimes it is somebody who should know better and other times it is someone who just does not know better! Just simply going in and saying "okay I can run a calculation," that is not that useful. Knowing when and what methodology to apply is very important.



The panel attempts to amicably settle a difference of opinion.

Patrick Holland: Is there a useful source of guidelines for establishing the "best" computational method?

Edwin Webster: Not really.

Patrick Holland: That is a pity. This could help reviewers and editors and others.

Edwin Webster: It is an alphabet soup. Some people may get disturbed when you say "alphabet soup", but that is what it is. It is alphabet soup. There are many competing methodologies and there are many caveats to using various methodologies. Furthermore, many of the limitations are not yet fully realized, which makes it even more difficult, especially for transition-metal and organometallic compounds. When one goes through the proper testing, calibration, and benchmarking of methodologies, you start down a road that really is no longer *Organometallics*, that is *Journal of Chemical Theory and Computation*. One wants to get the right answer for the right reason, not the "right answer" because it agrees with one's predilections. That is a big issue in computational chemistry,

getting the right answer for the right reason—or at least getting a good answer for an appropriate reason.

Patrick Holland: So you do not think it is feasible for there to be a set of journal guidelines?

Edwin Webster: There are easily identifiable items that make reproducibility more tractable. Many journals call for the inclusion of coordinates as a standard practice, but these coordinates do not always get checked. Furthermore, the SI does not always include these items, and that fact goes overlooked by reviewers.

Patrick Holland: This has been in the checklist for authors of papers in *Organometallics* for several years.

Edwin Webster: There still is not a standard procedure across all journals. Also, people put in things that obfuscate (intentionally or not). We should strive to make the process easier, not harder. There can be a hundred pages of coordinates. Does that really help you? Does that help the reviewer? Not particularly. I review things all the time, and I have to go through and get out coordinates and pull things out, and I find simple mistakes that were not made intentionally, but simple mistakes get made, and if I hadn't gone through every individual structure and pulled out the coordinates and convert the coordinates to a file that I can open in a 3-D viewer, the mistake might not have been found. These issues make the SI not as helpful as it could be.

Connie Lu: It would be great if there were something equivalent to CIF format (and also a checkCIF program) such that I could open up a three-dimensional image of a structure that someone had computed. By having a structure I could rotate or manipulate, I would learn so much more than from a 2D figure.⁵⁶

Edwin Webster: Note that the same burden is not necessarily there for experimentalists. If you synthesize a compound, you are ideally supposed to make it readily available to anyone who requests a sample. However, if you increase the burden too much, then some people are going to stop using computational chemistry as part of their toolkit because they might say it is too difficult to include all of these things the journal wants me to include. There is not yet an accepted standard for sharing computational results (like CIF for X-ray structures).

Robin Bedford: You are comparing computational chemists with experimentalists, but it would be better to compare them to crystallographers, who also deal with structural models. In crystallography it is a standard expectation that you have a CIF that can pass the appropriate checkCIF.

Edwin Webster: That is what I'm saying; the standard is not there yet for computational chemistry, and you are not going to get a consensus tomorrow on how to build it. A more challenging issue is that simply providing an input file will not necessarily lead you to the final result. I can provide you an input file that then fails—so what do you do then? The initial geometry used for the computation does not always actually produce the final result because many times one will have to tweak and change things—it is a process. I do put all of the final coordinates in the Supporting Information—these are my final output geometries—but if I just give you the final output as input, you could never reproduce what I actually did. Because there are so many parameters that go on in terms of spin state, SCF/wave function optimization, geometry optimization, different things that have to happen, it is its own science and some of it is black art, like finding transition states. In particular, I can give you the input file that I started out for trying to find a transition state and you'll never be able to find the transition

state I eventually found because searching for the transition state can take several iterations of input structures and input parameters. I could provide the final input file that got me there, but that is not where I started.

Patrick Holland: That does not bother me, because the situation is much like experiments. In an Experimental Section, I'm not describing the first time I did the reaction, I'm describing the time that it worked.

Edwin Webster: Giving output coordinates is the same as giving you the final structure. Simply supplying the input file with the coordinates of the first starting geometry is not necessarily useful. The final coordinates are obviously the final coordinates—they do not change, but for the input coordinates, there is a large variability of what can be produced by point and click to draw a geometry for what one might think it will look like. Then, you perform a geometry optimization, and there are technical details and these technical details can make a really big difference in terms of reproducibility of results. And then back to the accessibility of readable coordinates, and how do you go through and actually check what's there?

Robin Bedford: So what do you want? What would be the ideal for you?

Edwin Webster: I've thought about that, and that is one of the things with which we all struggle. You want a set of guidelines that produces a uniform format for final coordinates and energies (all raw energies should be listed) and easily identifiable ways of looking at 3D structures as Connie mentioned. You want those things that make it easiest to follow the chemistry. Using a set of 3D drawings from your favorite program in one given "best orientation" without labeling atoms or structures properly is less than ideal, and that is what oftentimes happens in publications. Another issue is the standardization of reporting program input parameters and basis sets. There are some available options, but these would require buy in from the journal editors and authoring community.

François Gabbai: Regarding the wish list on techniques for computations, I'd like theoretical chemists to develop better ways to take care of solvents. Right now, we only have methods such as the polarizable continuum model that do not account for specific interactions. Methods that could account for hydrogen bonding and other weak interactions would be a big step forward.

Edwin Webster: Currently, we can use a mixture of explicit and implicit solvation, but that is not necessarily ideal. We do need more robust methodologies for handling coordinating solvents and specific interactions.

François Gabbai: Yes, that would also be nice. Another one of my desires is in the domain of bonding analysis. The current practice is to use a number of methods, including AIM, NBO, and ELF. Because these methods sometimes give ambiguous results, it would be nice if the computational community could develop a more comprehensive and robust approach to bonding analysis.

Organometallics: On that note, we will conclude our second *Organometallics* Roundtable. The Editors would like to warmly thank all of the panelists for their time, engagement, and many valuable insights, and offer the hope that we will be able to convene again in 2015.

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Notes

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(56) Editor's note: a simple means of achieving this capability has now been implemented in *Organometallics*, as outlined in the 2014 Author Guidelines. See: Lichtenberger, D. L.; Gladysz, J. A. *Organometallics* **2014**, *33*, 835.

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