Green Chemistry: Cresting a Summit toward Sustainability

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Abstract:

As chemistry evolves, priorities must be identified and incorporated to guide chemists toward a sustainable future. When applied, the 12 principles of Green Chemistry deliver both environmental and economic benefit and logically should be adopted in every industrial and academic chemistry endeavour. In the main, this has not happened. While Green Chemistry philosophy has been generally accepted by the scientific community, technical Green Chemistry evolution through education, investment, and exemplification has yet to achieve the appropriate attention and effort. Three critical opportunities exist that can be used to redress this state of affairs and provide the necessary Green Chemistry evolution: improving engagement and support of business and academic leaders, enhancing education and technical guidance, and evolving toward proactive and pragmatic regulatory policies. Seizing these opportunities is an imperative start toward cresting a Green Chemistry summit that descends toward ultimate sustainability.

Introduction

Chemistry and chemical industries are evolving in the continuing human pursuit of longer life expectancy, higher quality of life, greater convenience, improved safety, and a broader understanding of the universe. Directing this evolution requires that priorities are identified to serve as guides preventing destructive forays down extinctive pathways and to refocus efforts toward positive evolutionary outcomes. Green Chemistry philosophy¹ provides a design for chemical evolution and a guide for scientists to accomplish sustainable practices during chemical research, development, and manufacturing. It has been proposed that evolution toward Green Chemistry has recently crested a summit² and gained momentum enough that general technical exemplification is both imminent and inevitable. Clearly, scientists better recognize and acknowledge the need for greater synthetic efficiency and environmental concern. Unfortunately, the scientific community as a whole has yet to commit the necessary resources to enable this higher level of efficiency through greener chemistry. What has been accomplished is a sea change in the attitude of many academic and industrial scientists, and a wide acceptance that the philosophy of Green Chemistry offers great potential economically and environmentally. So we have crested one Green Chemistry summit, the acceptance of guiding priorities for sustainability. The next summit will be crested through applied scientific research and technological advances guided by these priorities of sustainability. Three opportunities appear paramount in achieving this ascent. The first is proactive engagement by business and academic leaders providing direction and committing resources for Green Chemistry education and exemplification. The second involves retooling and enhancing current Green Chemistry education and providing guidance regarding approaches for the application of technical Green Chemistry. Finally, regulatory agencies must begin to redefine regulatory purpose to enable advanced scientific progress necessary for a sustainable future. These three opportunities provide a path forward to crest the next Green Chemistry summit.

The First Opportunity

There are numerous academic and industrial examples highlighting Green Chemistry application that have led to improved efficiency and subsequent improved economic and environmental performance.³ Why then do industrial and academic leaders resist implementing Green Chemistry principles and priorities?

Industrially, this may not be surprising. Corporate leaders are often trained in disciplines of business, law, or economics, but rarely hail from scientific backgrounds. The result appears to be a leadership class that does not fully trust the scientific method,⁴ a method which frequently produces nonlinear results difficult to predict and equally difficult to manage. There may also be confusion because no single definition for Green Chemistry exists, and full comprehension of the underlying principles of Green Chemistry is therefore minimal or even misguided. Though numerous case studies have borne out high efficiency when practicing Green Chemistry,³ many leaders do not appear to have accepted this as irrefutable truth. Some current leaders therefore appreciate the concept of Green Chemistry and the public relations opportunity it presents, but misguidedly avoid assuming the perceived risk and thus fail in enabling innovation. It may be that the seminal challenge for current industrial leadership involves a commitment to scientific excellence and a belief in scientific evolution as a true path to business superiority. There are isolated examples of this

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⁽⁴⁾ Schwartz, M. A. J. Cell Sci. 2008, 121, 1771.

leadership, but it is not general and is desperately needed by today's chemical industries that face not only significant scientific challenges but also globalization that is quickly eroding incentives for scientific evolution through the propagation of cost-cutting business models.

As an example, the current petroleum energy crisis was created by an analogous lack of leadership resolve. The low cost of petroleum provided a boon to the world economy for decades, but effectively masked the urgency for a sustainable solution to energy production. Research into alternatives was delayed, and potentially disastrous repercussions to society are the result today. A similar deficiency in long-term planning impedes Green Chemistry exemplification. For example, some research organizations have abandoned the pursuit of internal scientific excellence and rather elect to outsource research and manufacturing to developing nations where labor costs are relatively low and environmental and safety enforcement is lax.5 A temporary but artificial cost advantage is then created, and the inspirational economic drive for higher efficiency is eliminated without consideration of ultimate sustainability. In the short term, incentive for scientific superiority has been removed, potentially resulting in excess pollution, perpetuation of inferior methodology, and poor worker safety. The longterm ramifications may include the interruption of scientific progress, the dismantling of scientific infrastructure in developed nations, the deconstruction of a generation of functioning scientists, and the erosion of incentives for choosing scientific careers. Sustainability will not be achieved in this manner. Rather, there must be an expectation for ever higher operational efficiency during worldwide (internal or external) scientific operations which, at its core, will require a belief in the long term investment value of scientific excellence. Many business leaders have become reliant upon business models that temporarily minimize research expenses but fail to take into account the lost opportunities resulting from an interruption in scientific progress. The key component in a path to chemical business superiority, environmental responsibility, and long-term economic sustainability is leadership belief and support in the continual evolution toward scientific excellence. This must be supported and driven from the top down. Stronger support from industrial leaders beginning with investment in the exemplification of Green Chemistry principles can propel us to the next Green Chemistry Summit.

In academic settings, our leaders could make a terrific impact upon future sustainability by creating and propagating a Green Chemistry curriculum. There are isolated academic programs deeply committed to Green Chemistry principles,⁶ but this is not yet the norm. The delay may suggest a hesitancy to support the re-evaluation or even rejection of long-standing scientific priorities that Green Chemistry will incite. Perhaps Green Chemistry does not assert adequate interest and importance to academic leaders who have been trained in environments without concern for sustainability. Intellectual freedom remains paramount in academia, and scientific elegance is at times viewed as the novelty of initial discovery, as opposed to the most pragmatic or efficient solutions for scientific challenges. From this perspective, Green Chemistry may be perceived as a limiting force placed upon pure academic science which was previously free from consequence or boundary, acting to reign in creativity. On the contrary, bringing focus to chemical challenges through prioritization does not stifle but rather demands heightened creativity. Green Chemistry principles identify relevant chemical priorities and direct research efforts toward timely and significant endeavors. These priorities provide a broad new landscape for scientific exploration based upon new measures of chemistry success. In a brighter future, priorities of Green Chemistry will be incorporated into university curricula to provide direction, will be embodied within research grant expectations to drive and direct future innovation, and will become a significant part of the evaluation process used for peer-reviewed publication. In this future, Green Chemistry does not become a separate branch of science, but is rather the guiding philosophy for how all scientific goals are set, and how all scientific research and manufacturing are performed and evaluated. Academic leaders will play a critical role in the ascent to the next Green Chemistry summit. This will be a terrific challenge, and a unique opportunity to progress beyond outdated priorities in redefining the evolution of science within a context of sustainability.

Insufficient investment and inadequate intellectual value have been assigned to Green Chemistry endeavors by many current industrial and academic leaders. This in turn has led to limited motivation and direction imparted upon students and professional scientists due to nonsupportive leadership attitudes. What should an evolving scientist accomplish each day to achieve success both as a professional or student, and as a Green Chemist? Without leadership support and direction, each scientist is forced to decide how or even if they will incorporate Green Chemistry principles individually. The consistent, long-term, and overdue valuation and support of Green Chemistry principles through leadership in education, scientific training, career development, career advancement, strategic scientific partnerships, capital allocation, and most importantly, the setting of research goals and expectations comprise our brighter future and will propel us to the next Green Chemistry summit.

The Second Opportunity

The characteristics of each generation of scientists evolve in response to pertinent scientific challenges of their time. The current generation of practicing scientists must extend our standard of living while avoiding the depletion of natural resources and the poisoning of our environment, a challenge

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aimed at sustainability. Due to the broad but compartmentalized nature of modern science, defining applicable green technical solutions for every chemistry situation appears impossible. When scientists do become intent upon exemplifying Green Chemistry principles and are faced with the task of applying this philosophy in the actual performance of technical Green Chemistry, many become overwhelmed. As a starting point, the practitioner might consider two major technical Green Chemistry approaches.

Broad and General Technical Green Chemistry. The first approach is the broad and general exemplification of technical Green Chemistry. A powerful aspect of general, technical Green Chemistry is that it can be accomplished using current capabilities, requiring no new equipment or training. It is simply changing the way one thinks and the priorities that are set—not the technical solutions applied. In other words, new chemical techniques are unnecessary to achieve greener chemistry. Rather, it requires redirection of current techniques and capabilities within a new set of individual expectations. Each scientist must contemplate the 12 principles of Green Chemistry⁷ and exemplify those principles that directly relate to their specific scientific endeavor for improved relative efficiency. For instance, organic solvent accounts for greater than 80% of the waste during pharmaceutical synthesis.8 Ten liters of solvent for every kilogram of starting material in each chemical step is frequently deemed acceptable. By adjusting personal scientific expectations toward higher concentration and less solvent use, say half of this volume, tremendous Green Chemistry impact can be achieved. The largest component of process waste is minimized and reactor capacity maximized. Overall cost related to energy, waste disposal, solvent, facility and manpower is reduced, and no new technique is required to accomplish this greener chemistry. There will be cases when solvent volume cannot be reduced, but with the expectation of a new level of efficiency, average solvent use will diminish as opportunities previously overlooked are now seized. A new priority for higher efficiency and a rejection of the prevalent acceptance that dilute reactions are "good enough" is all that is necessary. This is but one example demonstrating that routine application of the priorities of the 12 principles of Green Chemistry enables a scientist to use established precedent and analysis of cause and effect to achieve broad and general exemplification of technical Green Chemistry. New technology and methodology will also be required for an evolution to sustainability, but broad and general Green Chemistry goes far to redefine the expectations of current scientific practice and can be performed with great and immediate impact.

Focused Green Chemistry. A second approach, focused Green Chemistry, also makes use of the 12 principles, but this time to identify areas where traditional and contemporary synthetic methodologies fail relative to said principles. This identification is followed by a search for *or creation of* alternative methodologies that can overcome these deficiencies. Put into other words, it is *changing your technical approach*

to achieve goals that are unreachable using current, synthetic methodology. For instance, issues of solvent volatility may be of critical importance, reaction selectivity may be insufficient, or energy use may be intensive in a chemical process. Standard technology and precedent have been applied, examined thoroughly, and found unable to sufficiently address these issues. One might then consider addressing solvent volatility using emerging science such as ionic liquids or perhaps efficient traps or condensers. If reaction selectivity is poor, perhaps supercritical fluid or biotransformation technology will increase efficiency. If a process is energy intensive, continuous flow processing may be more efficient if applied. The specific type of technology is unimportant. The importance of focused Green Chemistry is rather making use of or creating new technology to overcome limitations in current methodology and processing that will ultimately deliver superior performance as judged by the priorities of the 12 principles of Green Chemistry. Academic efforts will not be exclusive but will likely predominate in building the chemistry toolbox of the future. Industrial chemists on the other hand, must proactively exemplify and generalize these techniques to accelerate the evolution of scientific excellence.

The goals of focused Green Chemistry are the replacement of traditional methodologies that fail the priorities of the 12 principles, the continued expansion of general scientific capabilities toward higher efficiency, and access to novel chemical transformations.

The Third Opportunity

A critical third opportunity for cresting the next Green Chemistry summit involves the current roles and relationships between regulatory agencies and those that they regulate. Assessing the risk in approving a product for public use involves both philosophical and pragmatic issues concerning acceptable human and environmental risk, and whether the need for or potential benefit of a product outweighs the potential consequences of use. Therefore, a powerful urge to limit unintended consequences (and hence innovation) exists in all regulatory agencies. It is important to recognize philosophically that *there is less risk of harm in pursuing positive scientific evolutionary paths through innovation than in propagation of paths that are ultimately unsustainable*.

It has been stated that fear and surprise drive regulatory responses,⁹ so it is critical to continually examine and discuss the evolution of current or suggested regulatory policy and the likely impact. One regulatory approach involves the potential requirement for chemical firms to provide toxicological data regarding every chemical currently used, enabling regulators to better grade chemicals individually.¹⁰ Predicting chemical toxicity to humans and potential unforeseen chemical effects in our environment is an imperfect science even when practiced by the most gifted toxicologist. Extensive and expensive testing to obtain meaningful empirical data is required, and when does

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⁽¹⁰⁾ Panel Discussion: 2nd International Symposium on Green Processing in the Pharmaceutical and Fine Chemical Industries, Yale University, New Haven, CT, May 2008.

the testing end? Which become more important, hormonal or mutagenic effects, liver toxicity, or renal implications? Each require different and expensive animal models including tests based upon differing mechanisms of toxicity, and how does one account for the overall effects of chemical mixtures in a human or in the environment? Currently, the Toxic Substance Control Act (TSCA), and Registration, Evaluation and Authorization of Chemicals (REACH) exist as regulatory examples in the United States and the European Union that serve to guide appropriate toxicological examination.11 A further extension of industrial requirements to theoretically enable regulators to routinely assess every chemical and its chemical toxicology at this time in an ad-hoc fashion is unrealistic and economically prohibitive and will ultimately prove unreliable. As for novel chemicals, they should continue to be assessed when a product has reached an advanced stage and merits such investment and scrutiny. This is not to suggest precluding the use of current toxicology in the design of safer chemicals but rather serves to highlight the difficulty and potential harm of regulating chemicals through application of broad, ill-conceived policies.

Some have also suggested that extensive training and a deep understanding of toxicology on the part of chemists should be pursued as well.¹² A better approach is to train chemists to be more efficient chemists! *Focus upon synthetic efficiency will minimize the overall and unnecessary burden of <u>all</u> excess chemicals in the environment.*

Some feel it is the role of regulators to guarantee that each new chemical product is harmless. Should this be the case? Every chemical in large enough quantity becomes a poison. Perhaps enabling informed decisions by customers and patients regarding the potential positive and negative outcomes is adequate. Who determines acceptable risk when no therapeutic options exist? If a product provides benefit to 99.9% of the population but deleterious effects upon the remaining 0.1%, should the larger group be deprived of access to this product? There are no simple answers to these questions, but better communication is critical for regulatory evolution to occur.

Consider pharmaceutical manufacture and Green Chemistry. A number of carefully controlled synthetic steps are required to synthesize an active pharmaceutical ingredient. By defining these "regulatory" steps early, pharmaceutical firms hope to accelerate drug approval and maximize patent life. Clinical testing is performed using drug generated via early synthetic methodology. If a superior method of chemical synthesis is discovered post clinical testing, regulators introduce procedural hurdles and/or additional toxicity study requirements prior to allowing use of the more efficient methodology. Pharmaceutical firms generally opt to stay with approved but inefficient chemical processes to avoid these costly penalties and the risk and expense of additional clinical study. Should extensive and expensive toxicological studies be required to allow pharmaceutical manufacturers to use new, superior chemical methodology if drug characterization is possible using advanced analytical methods? Should product patent life be extended to companies that invest in sustainability through superior methodology to encourage further investment? Should methodology be granted intellectual property protection based purely upon Green Chemistry measures?

At this time, solutions are not clear. What has become clear is that regulatory agencies play a much larger and ever increasing role in the propagation or prevention of superior emerging science than ever before. Regulatory policy therefore needs to adopt a more proactive and far-sighted approach. Part of this must be the re-examination of regulatory purpose. Acting as a proponent and guide in stewarding scientific evolution is in the best public interest for the long-term. For the betterment of society, regulators must encourage the evolution of modern science by enabling new technology and better methodology for general and approved use faster and without penalty.

Conclusions

A summit has been crested with regard to the general scientific acceptance of Green Chemistry philosophy. We are now surrounded by soaring peaks of Green Chemistry application and exemplification that we must scale to fully embrace the philosophy of Green Chemistry to reduce it to practice. The evolutionary success of academic and industrial chemistry will depend greatly upon priorities selected to guide innovation during this critical ascent. These priorities must be firmly rooted in the 12 principles of Green Chemistry to facilitate a path to sustainability. To realize this path, business and academic communities must seize three critical opportunities. First, leaders must strive to champion the propagation of Green Chemistry principles and practices from the top down. This can be accomplished industrially by expanding Green Chemistry expectations and through expanded research investment to enable and inspire technical exemplification. Academically, a Green Chemistry culture can be created through higher expectations of sustainability taught via new curricula, and updated textbooks incorporating the 12 principles. This exemplification must become a primary leadership goal predicated upon a belief in the long-term advantage of superior, evolutionary, sustainable science. Second, current technical chemistry practitioners must achieve a deep understanding of Green Chemistry principles to enable specific, situational application of broad and general as well as targeted technological Green Chemistry for higher synthetic, economic, and environmental efficiency. Third, regulatory agencies must ensure public and environmental safety while proactively encouraging and enabling the use of superior scientific methodology for the advancement of science and the ultimate benefit of society. Seizing these opportunities will provide stronger footholds for technical Green Chemistry ascent and perhaps reveal a tractable path for cresting a summit that leads to sustainability.

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⁽¹¹⁾ See Chemical Regulation: Comparison of U.S. and Recently Enacted European Union Approaches to Protect against the Risks of Toxic Chemicals, GAO-07-825, September, 2007; http://www.gao.gov/ products/GAO-07-825.

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