Organic Process Research & Development

EDITORIAL

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Sustainable Process Chemistry

The past decade has witnessed an exponential growth in process chemistry knowledge. It is difficult to imagine modern life that is not touched by some facet of process chemistry. One of the key facets is Sustainable Process Chemistry—a scientific concept that encompasses the improved protocols for efficient, effective, and safe manufacturing of chemical products. This includes design, manufacture, and use. Process chemists in academia and industry have been busy developing processes that are able to mitigate the risk and prevent pollution while minimizing the waste during various stages of the production of chemicals. Sustainable Process Chemistry has stimulated innovations across all disciplines of chemistry where human health and environmental harmony is protected.

In 1992 during the United Nations Conference on Environment and Development in Rio de Janeiro (Earth Summit), the concept of Sustainable Development was established. The overall impact of this concept has been extraordinary in shaping the philosophy of Green Chemistry—a term coined by the Environmental Protection Agency (EPA) of the United States.

> "To promote innovative chemical technologies that reduce or eliminate the use or generation of hazardous substances in the design, manufacture and use of chemical products."

These efforts have culminated into the 12 principles of Green Chemistry by Anastas and Warner that are now widely accepted as the main framework of Sustainable Chemistry. Therefore, Green Chemistry and Sustainable Chemistry convey the same message that is also applicable to Sustainable Process Chemistry. Herein, seven articles have been assembled on the Sustainable Process Chemistry elaborating the increasing importance of this discipline.

Abbreviated Version of the 12 Principles of Green Chemistry

(Adapted from *Green Chemistry: Theory and Practice*; Oxford University Press: NY, 1998.)

(1) Prevent pollution and waste
(2) Design safer chemicals and products: atom economy
(3) Design less hazardous chemical syntheses
(4) Design safer chemicals
(5) Use safer solvents and auxiliaries
(6) Increase energy efficiency
(7) Use renewable feedstocks
(8) Reduce derivatives
(9) Use catalysts, not stoichiometric reagents
(10) Design for degradation
(11) Analyze in real-time to prevent pollution
(12) Minimize the potential for accidents

The first article by Jiménez-González et al. is unique because it is coauthored by scientists from the American Chemical Society (ACS) Green Chemistry Institute (GCI) and eight major global pharmaceutical companies describing their perspective on the key Green Engineering research areas for sustainable manufacturing. In 2007 this group of scientists had a conference identifying and recommending top Green Engineering research areas highlighting their challenges and opportunities. Therefore, we are delighted to see that this article sets the tone for this special issue and the message that we wish to convey.

The second article is also authored by Jiménez-González from GlaxoSmithKline (GSK) and coauthors Broxterman from DSM and Manley from ACS GCI. This article goes into further details of the green metrics and their recommendations for selecting process mass intensity (PMI) or mass efficiency over more traditional metrics such as E-factor and atom economy. The authors believe that PMI would be a reliable high-level metric that is easy to generate and compare the greenness of a process route with the least investment of time and efforts.

The article by Greek authors Vasiliadoua and Lemonidoua describe their efforts and success with the glycerol hydrogenolysis to propanediols using Ru/SiO_2 catalyst. Interestingly, glycerol has been identified by the U.S. Department of Energy as one of the top 12 building-block chemicals that can be derived from biobased feedstocks and converted to high-value biobased chemicals or materials. Therefore, this article is expected to advance the seventh principle of the Green Chemistry.

The article by Bourne et al. elaborates on the process optimization for methylation of alcohols in supercritical CO_2 using a continuous flow reactor. The process of methylation of 1-pentanol was monitored by online GC, enabling efficient process control without human intervention. The use of automation and design of a continuous flow reactor exemplifies the sixth principle of Green Chemistry.

Storz and coauthors from Pfizer have studied chloroimidate cyclization, furnishing an elegant and straightforward synthesis of 4-chloropyrimidines. Their contribution describes a one-pot protocol for several chloropyrimidine analogues that are traditionally synthesized via a multistep procedure. Implementation of such processes is believed to reduce waste (first principle of Green Chemistry) and increase sustainability.

Yet another article, contributed by the Pfizer group of scientists, describes kilo-scale diastereoselective synthesis of norbornyl carboxylic acid from norbornylene, employing low-pressure hydroformylation. Herein, Gu et al. describe the use of *tert*-butanol as a solvent of choice and selection of low-loading ligand (dppf) for hydroformylation. This article fulfills the ninth principle of Green Chemistry related to the use of catalytic amounts of reagents.

The last article in this special issue, describing the toxicological study of 2-methyltetrahydrofuran (MeTHF) and cyclopentyl methyl ether (CPME), is contributed by Antonucci and coauthors from Merck. The authors conclude that use of MeTHF and CPME as solvents in the early development phase of active pharmaceutical ingredient (API) synthesis would be safe at low levels (<2%). These solvents are considered as negative for genotoxicity and mutagenicity, supporting the third principle of Green Chemistry.

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Clearly, the design and implementation of Sustainable Process Chemistry will continue to play a vital role in the success of the chemical industry. These articles further confirm the active research into alternative technologies that deliver improved chemical synthesis protocols. We hope that this special issue will further catalyze the research in this area and readers will consider publication of their future work in OPRD.

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