NEW VOICES IN CHEMISTRY

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THE INCREDIBLE POWER OF ORGANIC SYNTHESIS

Synthetic chemists will be needed to produce increasingly complex molecules in many fields

"THUS SYNTHESIS EXTENDS ITS conquests from the elements up to the domain of the most complicated structures ...." With this statement, French professor and senator Marcellin Pierre Eugene Berthelot took his place in history as one of the first organic chemists to recognize the incredible power that synthesis would hold for years to come. Indeed, it is this characteristic of organic synthesis that drives many chemists, including me, to delve into this challenging but rewarding area of chemistry.

Many people have said that organic synthesis is a mature science, and I agree with that statement if "mature" is taken to mean simply that we have methods for making the majority of functional arrays found in natural products or other sought-after compounds at our disposal. However, "infancy" is the best description of organic synthesis if one adds to this description the challenge of efficiency, and more so if it is coupled with the requirement of preparing a single enantiomer using only catalytic quantities of chiral promoters.

In fact, entire classes of compounds lack efficient asymmetric methods for their synthesis and also require additional exploration of their utility and synthetic potential. This challenge is what drives my group's interest in b-lactones (2-oxetanones). Thus, it appears that the need for improved efficiency and the quest for new reactivity will continue to drive basic research in organic synthesis.

Total synthesis remains increasingly challenging as the complexity of targets escalates and the demands of efficiency and conciseness become justifiably more important. Perhaps we have done our science a disservice, as some other have noted, in beginning our discussions of total syntheses as descriptions of well-laid-out plans that proceeded as predicted or anticipated. We speak of preconceived retrosyntheses that often are only forward syntheses written backwards! In fact, even the most well-laid-out synthetic plans give way to the unexpected, and indeed, the unexpected is what makes our science exciting! There is always the possibility—and the likelihood—that an alert practitioner will discover an unexpected reactivity of a functional array in the course of a total synthesis. This potential for the serendipitous discovery of novel reactivity will undoubtedly fuel future endeavors in total synthesis.

TOTAL SYNTHESIS **Romo (right) discusses research results with graduate students (from left) Karine Poullennec, Min Zhou, and Anja Dilley at a sub-group meeting.**

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Nature continues to provide synthetic chemists with an overwhelming diversity of natural products that inspire us to stretch our imaginations, driving the development of new strategies and tactics for the assembly of these often biologically relevant metabolites. Natural products have been at the forefront of melding the fields of organic chemistry and biology, and the fields will only continue to come together in the future. For example, marine organisms have recently received more attention because of the diversity of sessile organisms that have developed chemical means to defend themselves. These chemical warfare agents continue to be useful lead compounds for cellular studies and drug development. However, an undesirable result of combinatorial or massive parallel synthesis is the notion that "true" diversity could be found in such approaches.

However, it seems that it will be some time before chemists will be able to compete with nature in assembling atoms in such unique and unexpected ways. These often-spectacular arrangements of atoms invoke the creativity of organic chemists to develop efficient syntheses that enable further investigations into their cellular effects. There also has been recent interest in manipulating the biosynthetic machinery to vary the structure of "natural products." This approach may become one way to harness the diversity that nature achieves in a seemingly effortless manner.

In the coming years, synthetic organic chemists will continue to redefine themselves, and fresh new opportunities for applying their expertise will continue to arise. In fact, the art of making molecules is a valuable commodity in the areas of biology and materials, and as a result, synthetic chemists will continue to find themselves in high demand in various branches of science.

Finally, basic research in organic synthesis must continue to keep in step with the need to synthesize increasingly complex target molecules and the need to have at our disposal synthetic methods that are characterized by greater ease and efficiency. These fundamental exercises coupled with the many avenues available for applying organic synthesis will continue to foster creative works in this area throughout the 21st century.

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