

PREFACE TO VOLUME 87

Synthetic chemists have been defining a “complex molecule” in the way that many people define art: they know it when they see itthe size, symmetry, branching, rings, multiple bonds, and heteroatoms [are the] characteristics of a complex molecule.

S. Bertz, *J. Am. Chem. Soc.* **1981**, *103*, 3599

The reactions that comprise the three chapters in this volume share the common feature of significantly increasing molecular complexity. Over the years, many synthetic chemists have described molecular complexity in somewhat vague and intuitive terms and some, most notably Bertz, have attempted to define it using more rigorous, even mathematical treatments. Nevertheless, we still know it when we see it and scanning the contents of this volume will no doubt inspire the reader to acknowledge that all of the transformations covered introduce substantial complexity from starting material to product.

The first chapter authored by Pedro Merino describes the manifold ways in which the latent functionality embedded in the humble heterocycle furan can be revealed by various oxidative processes. Through the action of oxygen, halogens, chromium(VI), and other oxidants, furans are efficiently converted to a myriad of 1,4-dicarbonyl compounds as well as oxygenated butenolides. The ready availability of these building blocks provides a straightforward solution to the problem of “dissonant” carbonyl relationships, i.e. those not constructed by classical carbonyl condensation chemistry. A second oxidative transformation is of such general utility that it has achieved the exalted status of a name reaction, the Achmatowitz reaction which converts furfuryl alcohols into 6-hydroxy-2*H*-2-pyranones. This oxidation (and its aza analog which furnishes 2-pyridones) is applicable to a wide variety of substituted furfuryl alcohols, allowing access to a range of substituted products. Many different oxidizing agents have been employed for this process, including bromine, peracids, iodine(III) reagents and *tert*-butyl hydroperoxide under vanadium(IV) catalysis. This variant has found extensive application in total synthesis endeavors; moreover the hydroxy-pyranones serve as precursors for oxidopyrrolylium ylides which can engage in [5+2] cycloadditions. Finally, the furan nucleus can serve as a masked carboxylic acid, normally unveiled under the action of ruthenium tetraoxide. Although not particularly complexity generating in this capacity, it nonetheless serves an important role in synthesis planning. Prof. Merino has provided a thorough illustration of the usefulness of simple furans and an excellent guide to selecting the appropriate oxidizing conditions for a specific transformation.

The second chapter authored by Nanyan Fu and Thomas T. Tidwell details the fascinating cycloaddition and electrocyclozation chemistry of unsaturated ketenes.

The highly reactive intermediates (vinyl-, allenyl-, and alkynylketenes) can be generated in situ from a host of readily available precursors such as carboxylic acids, cyclobutenones, diazo ketones, and benzoquinones, usually by irradiation or thermolysis. Once formed, these unsaturated ketene derivatives undergo a variety of transformations depending upon the presence of other 2π components either tethered to the substrate or added separately. If the appended 2π component is an alkene, then simple electrocyclozation takes place to form aromatic compounds (phenols) or in the case of appended alkynes, phenolic 1,3-diradicals form that undergo subsequent cyclizations or rearrangements. In situ generated vinyl ketenes can engage as 4π components in Diels-Alder reactions or as 2π components in thermally allowed [2+2] cycloadditions to form cyclobutanones. In addition, many of these transformations have been engineered into substrates that are capable of undergoing cascade-type reactions that construct polycyclic structures with a dramatic increase in molecular complexity. Not surprisingly, therefore, these reactions have enjoyed great success in the synthesis of natural products, particularly condensed, polycyclic, aromatic compounds. Dr. Fu and Prof. Tidwell have done an outstanding job of compiling the various methods of generation of the unsaturated ketene precursors and illustrating the remarkable diversity of ring-forming processes that are available by judicious choice of addend. This chapter represents Prof. Tidwell's second contribution to the *Organic Reactions* series (Volume 39, Chapter 3) and we are grateful for his efforts in providing another excellent treatise on a topic he knows well.

The third chapter authored by Genia Sklute, Hannah Cavendar, and Ilan Marek chronicles the development of a remarkable organometallic reaction of unactivated alkenes and alkynes, namely carbozincation. Carbometalation reactions are known for many different metals, but the most noteworthy features of carbozincation are the mildness of the reaction conditions and the synthetic utility of the resulting organozinc products. Straightforward carbozincation of alkynes affords geometrically defined alkenes in a very useful way, but the more useful (and more complexity generating) transformation is the subsequent addition of the primary organozinc product to tethered alkenes in a metallo-ene process. Furthermore, the secondary organozinc product can be engaged in many carbon-carbon or carbon-heteroatom forming reactions including cross-coupling, halogenation, stannylation, or sulfenylation. Among the more remarkable variants of this process is the carbozincation of alkenylmetallic (lithium, magnesium, zinc) compounds to generate 1,1-dimetallalkyl derivatives. These unusual reagents react sequentially with different electrophiles to generate geminally functionalized products. Given the low cost, functional group tolerance, and ease of preparation of organozinc precursors, the carbometalation reaction is destined to attract the attention of synthetic chemist in industrial and academic settings. Prof. Marek is a world-renowned expert in organozinc chemistry and he, together with his former student Prof. Sklute and her student, Ms. Cavender have composed a definitive guide for researchers interested in harnessing the power of organozinc compounds in complexity generating processes.

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