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Introduction: Cyclopropanes and Related Rings

Why would a thematic issue deal with small rings and their chemistry? Nearly 120 years after the first synthesis of a cyclopropane derivative—in 1884 by William Henry Perkin, at that time working as a young visiting scientist (or a postdoctoral fellow in current terms) in the laboratory of Adolf von Baeyer in Munich, Germany—there remains among chemists a significant degree of curiosity about how far we can get a carbon atom and its homologues to bend their preferred bonding angles and accommodate unusual bonding situations. Thus, there is always a bonding theoretical aspect associated with novel highly strained and/or oligocyclic small-ring compounds. Furthermore, there is still a lot of new small-ring chemistry in terms of theoretically interesting molecules being published. There is even more small-ring natural products chemistry being uncovered. While the presence of three- and four-membered carbocycles in many terpenes has been known for more than half a century, nobody would have anticipated the discovery of oligo-unsaturated fatty acids with four and even five continously linked cyclopropyl groups, or the discovery of an octapeptolide containing two molecules of a 2′-nitro-substituted cyclopropylalanine. In addition, the chemistry of cyclopropyl-group-containing amino acids, whether natural products or analogues of naturally occurring amino acids, has advanced tremendously in the past 20 years. Many of these amino acids and their various derivatives have interesting and important biological activities, and no pharmaceutical research laboratory today will forget to attach a cyclopropyl group instead of an isopropyl or a *gem*-dimethyl carbon moiety to a physiologically active molecule, especially when adjacent to a nitrogen atom. In fact, the patent literature lists over 200 pharmaceutically relevant compounds containing a cyclopropylamine moiety. The broad-spectrum antibiotics Ciprofloxacin, Trovafloxacin, and Moxifloxacin are probably the best-known examples. Such developments undoubtedly are going to continue, and thus it appears timely to address several topics of current and future interest in small-ring chemistry in this thematic issue of *Chemical Reviews*.

According to one possible credo, "Let theory lead the way", an article by Paul Rademacher on photoelectron spectra of cyclopropane and cyclopropene derivatives sheds some light on the bonding theoretical aspects of such compounds.

Tremendous advances have been made in the stereoselective synthesis of cyclopropane derivatives in the past 20 years. This becomes evident in the contributions by André B. Charette with co-authors Hélène Lebel, Jean-François Marcoux, and Carmela Molinaro on stereoselective cyclopropanation reactions, and by Jörg Pietruszka on the synthesis and properties of oligocyclopropyl-containing natural products and model compounds.

Many fluorinated cyclopropanes and cyclopropenes have peculiar properties, both physical and chemical. These are compiled in an article by William R. Dolbier, Jr., and Merle A. Battiste. The ready availability of *gem*-dihalocyclopropanes—prepared by dihalocyclopropanation of alkenes—and their versatile transformations make them useful building blocks for organic synthesis, as is evident in the review by Michał Fedoryński. One of these widely applicable transformations is their conversion to allenes upon treatment with alkyllithium reagents. Recent advances of this 40-year-old methodology are presented in the article by Leiv K. Sydnes. Donor−acceptor-substituted cyclopropane derivatives form another family of particularly versatile building blocks for organic synthesis, and Hans-Ulrich Reissig and co-author Reinhold Zimmer make this a convincing point in their contribution. Also along these lines of synthetically applicable reactions are the thermal rearrangements of vinylcyclopropanes to cyclopentenes, although the corresponding article by John E. Baldwin emphasizes the mechanistic details underlying this transformation, since the preparative aspects have been reviewed in this journal and other periodicals several times in recent years.

Thermal rearrangements also play key roles in the application of 1,3-dipolar cycloadditions to alkylidenecyclopropanes and subsequent transformations of the resulting products to interesting heterocycles, as described by Alberto Brandi with co-authors Stefano Cicchi, Franca M. Cordero, and Andrea Goti, and in the [2 + 1] cycloadditions of vinylcarbenes generated by thermally induced cyclopropene ring opening, as summarized by Mark S. Baird. An analogous ring opening is also one of the synthetically useful reaction modes of cyclopropenone acetals, the

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preparation and chemistry of which are reviewed in a masterly fashion by Eiichi Nakamura with co-authors Masaharu Nakamura and Hiroyuki Isobe.

The succeeding set of three contributions deals mainly with molecules of theoretical interest, such as the cycloproparenes, compiled by Brian Halton, the cyclopropenylium cations, cyclopropenones, and heteroanalogues, summarized by Koichi Komatsu with co-author Toshikazu Kitagawa, and heavy cyclopropenes of Si, Ge, and Sn—a new challenge in the chemistry of group 14 elements—presented by Akira Sekiguchi with co-author Vladimir Ya. Lee in the most up-to-date review.

Edward Lee-Ruff and co-author Gabriela Mladenova focus on four-membered rings in their review on the use of enantiomerically pure cyclobutane derivatives as building blocks in organic synthesis. A more general overview of various reaction modes of cyclobutanes and cyclobutenes, applicable in organic synthesis, is that by Dieter E. Kaufmann and co-author Jan C. Namyslo. Cyclobutarenes and related compounds, another class of theoretically interesting molecules, are the subject of the contribution by W. Edward Billups with co-authors Anil K. Sadana and Rajesh K. Saini.

Two articles on cyclopropane chemistry relating to natural products conclude the round dance. Oliver Reiser and co-author Frieder Gnad summarize syntheses and applications of β-aminocarboxylic acids containing a cyclopropane ring in peptides, while Ludger Wessjohann and co-authors Wolfgang Brandt and Thies Thiemann engage themselves in the biosynthesis and metabolism of cyclopropane rings in natural compounds. This multifaceted review of current knowledge in this area clearly demonstrates that research is far from being at an end, and this definitely holds true for all the other areas of small-ring chemistry addressed in this thematic issue. Due to the limited space available, this volume does not cover all important aspects of this flourishing field. Further "state-of-the-art" contributions, written by experts in each area, will appear in regular volumes of *Chemical Reviews* in the future.

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