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BOOK REVIEWS

Heterocyclic Scaffolds I: β-Lactams. Edited by Bimal K. Banik (University of Texas−Pan American, Edinburg, TX, USA). From the series: Topics in Heterocyclic Chemistry, Volume 22. Edited by Bert U. W. Maes. Springer-Verlag: Berlin, Heidelberg. 2010. xii + 380 pp. $409. ISBN 978-3-642-12844-8.

β-Lactams incorporate all the elements of privileged scaffolds, mechanism-based enzyme inhibitors, and theoretically interesting strained molecules. Thus, it is not surprising that research on this heterocyclic system continues at an accelerating pace. This monograph on the β-lactam scaffold, the latest in the Topics in Heterocyclic Chemistry series, does an admirable job of covering recent developments, with emphasis on the development of new synthetic strategies and their use in the preparation of fused bicyclic, spirocyclic, and solid-phase libraries of β-lactams.

The first chapter covers the preparation of spirocyclic and fused β-lactams, especially the use of transition-metal mediated processes to close the adjoining non-β-lactam ring. The chemistry described is elegant, employing a wide array of chemical processes. References cover the literature through 2008. The second chapter focuses more narrowly on spirocyclic β-lactams, which represent a class of molecules with substantial biological activity, including uses as inhibitors of cholesterol absorption, antivirals, antibacterials, and β-turn mimetics. This is followed by an extensive chapter on the synthesis and applications of β-lactams that covers the past decade and focuses on the synthesis of the four-membered heterocycle itself. The most commonly utilized synthetic approaches are adequately covered, including the Staudinger, Gilman-Speeter, Alper, Mitsunobu, Kinugasa, and Torii reactions. Approaches involving a wide array of intramolecular cyclizations, including those employing electrochemical, photochemical, ultrasound, basic, and acidic conditions, are also covered. The chapter is well written, thorough, and extensively referenced. It ends with an overview of the biological activity of β-lactams, with coverage of their use as inhibitors/antagonists of a number of biological targets, including β-lactamase, nonconventional bacterial targets, human leukocyte elastase, cysteine proteases, thrombin, vasopressin V1a, cholesterol absorption, HCMV protease, and β-lactams that exhibit anticancer activity. While the last third of the chapter overreaches a bit, it provides lead references to a number of interesting applications nonetheless. Although both the first and second chapter are well written and representative of their perspectives, it might have been more appropriate to start the book with the contents of the third chapter, which provides a broad overview of synthetic strategies and biological applications, and then follow with the more specialized content of the spirocyclic and fused β-lactams.

A subsequent chapter on the use of β-lactams in the preparation of amino acids is very well written and provides a useful survey of recent developments in this important area. Consistent with the thorough treatment of the other reviews, this chapter covers all possible ring-openings of β-lactams, including N_1-C_2, C_2-C_3, C_3-C_4, and N_1-C_4. The book concludes with sections on the generation of solid-phase libraries of β-lactams, computational studies on the thermal [2 + 2] cycloadditions leading to β-lactams, and a chapter in which the personal research of the editor on the development of new anticancer β-lactams is described. The chapter on solid-phase applications covers recent developments leading to monocyclic β-lactam libraries, utilizing the Staudinger, Gilman−Speeter, and Miller's hydroxamate approaches. There is also a short discussion of approaches to penam libraries, where the progress has been slower, undoubtedly due to the high, and sometimes unpredictable, reactivity of these bicyclic scaffolds. The computational chapter considers both the Staudinger (ketene + imine) as well as the alkene + isocyanate pathways.

Overall, this volume constitutes a systematic, thorough, and densely packed compendium of recent synthetic developments in the β-lactam area and should be of use to anyone wishing to pursue research in this field. The individual chapters are organized, thorough, and up to date, with most including references up to 2008. Given the demonstrated biological relevance of this heterocyclic system, I believe we are likely to see more developments, both synthetic and pharmaceutical, in the coming decade.

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