Intramolecular and Transannular Diels-Alder Reactions

Few reactions can compete with the Diels-Alder (DA) [4+2] cycloaddition for the rapid and efficient generation of molecular complexity. The DA reaction is atom-economic and stereospecific, as well as diastereo- and regioselective. The intramolecular version (IMDA) of the DA cycloaddition and its transannular (TADA) counterpart are the subjects of this chapter, which covers major advances made since the first edition of Comprehensive Organic Synthesis. The chapter deals first with type 1 and type 2 IMDA cycloaddition, with a discussion on the effect of the nature of the tether linking diene and dienophile, methods for acceleration of IMDA reactions (such as use of high pressure) and catalysis (using oxophilic or carboxylphilic metal complexes, Brønsted acids, and enzymes). The use of furans as diene components (IMDAF), intramolecular hetero-DA (IMHDA) and IMDA reactions with inverse electron demand are also covered. Applications of IMDA to asymmetric synthesis (from substrate control through to enantioselective catalysis, including organocatalysis) are presented, along with tandem sequences involving IMDA cycloaddition. A theme pervading the whole chapter is the use of IMDA reactions for the total synthesis of complex natural products, including syntheses designed on the basis of biosynthetic proposals. The chapter concludes with an overview of the TADA cycloaddition, again with emphasis on recent total syntheses. © 2014 Elsevier Ltd. All rights reserved.