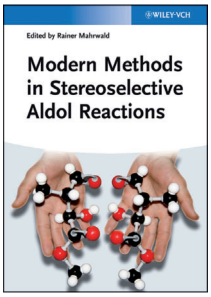
Modern Methods in Stereoselective Aldol Reactions



Modern Methods in Stereoselective Aldol Reactions
Edited by Rainer Mahrwald.
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The aldol reaction has few competitor reactions when it comes to the efficient synthesis of many polyketide natural products. The aldol reaction gives products with up to two new chiral centers and when used in an iterative manner it can rapidly give access to polyacetate or polypropionate units. Anybody venturing to make a polyether, a macrolide antibiotic, or a natural product containing polypropionate units must be versed in the different methods to make aldol products stereoselectively: chances are one or more aldol reactions will figure in the synthetic strategy. In that regard, the book *Modern Methods in Stereoselective Aldol Reactions* edited by Rainer Mahrwald provides all the necessary information. The eight chapters cover most known methods, each chapter replete with instances of uses in the synthesis of natural polyketides and other natural products. The title of each section of the eight chapters can be found at the beginning of the book. The index, however, should have been somewhat larger.

Chapters five and six describe all of the stereochemical features of an aldol reaction and all the necessary concepts needed to understand the challenges in controlling those elements. For that reason, they should have been placed as the first and second chapters. They also provide a "map" of the different controlling elements, and discuss each in depth. Chapter five is concerned with asymmetric induction in the aldol reaction and chapter six describes the substrate-controlled synthesis of polypropionate units. The latter covers exhaustively every aspects of the propionate aldol reaction, including the stereocontrolling elements in Zimmerman–Traxler and open chain transition states. It also discusses the double stereodifferentiation concept. This information is useful when reading the other chapters where many of the stereocontrolling elements are displayed but not necessarily explained.

Chapter one describes the special case of the "acetate aldol" in depth, including the Mukaiyama aldol variant. The stereochemical features are not different from the propionate aldol reaction but controlling them in this type of substrates poses an additional challenge because of diminished interactions due to the lack of substituents at C2 on the enolate. The chapter starts with a brief historical perspective and has examples of the use of each method in the total synthesis of natural products. Many references to older literature in that chapter help the reader get a sense of the evolution of the different methods. However, more comparisons with its cousin the "propionate aldol" may have been helpful.

Chapter two describes the vinylogous Mukaiyama aldol reaction and its many variants. This reaction is complicated by its "open-chain" transition state and the fact there are two possible reacting sites, which makes controlling the regiochemical and stereochemical outcome difficult. The sections of that chapter are arranged in a logical order by structure of the dienolate, which makes it easy to follow. A synthetic organic chemist would easily find the method appropriate to his or her particular substrate.

Chapter three is the largest and is concerned with the organocatalyzed aldol reaction. It is a genuine history of the method, starting from the discovery of the proline-catalyzed conditions by the Schering and Hoffmann-La Roche groups to recent proline derivatives and phase-transfer methods.

The so-called supersilyl protective group, tris(trimethylsilyl)silyl, allows for very interesting iterative mixed aldol sequences, some in one-pot procedures. The breadth of this strategy is clearly covered in chapter four. Good explanations of the stereochemical outcome of the given examples abound and help the reader appreciate this useful variant of the aldol reaction.

Tying the metal enolate to a chiral auxiliary is perhaps still the most utilized method to make chiral non-racemic aldol products. This subject is exceedingly well covered in Chapter seven. Although only oxazolidinones, oxazolidinethiones, thiazolidinethiones, and imidazolidinones are discussed, all concepts of mechanism and asymmetric induction are included and are relevant to many other chiral auxiliaries.

Chapter eight introduces the reader to an interesting alternative method, namely the enzyme-catalyzed aldol reaction. This method is complementary to all others with respect to the kind of starting substrates it transforms. The level of chiral induction is, without surprise, almost perfect. The authors cover the latest developments in this field, which has grown substantially in the last decade or so as well as instances of use in the synthesis of biologically relevant compounds.

Overall, this is an excellent book. It is centered on the application of the aldol reaction in total syntheses, which will please the synthetic organic chemist. Its chapters describing all of the fundamental concepts and the exhaustive coverage of the methods will satisfy both novices as well as experts.

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