CHEM 330

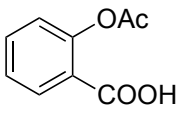
Topics Discussed on Sept. 9

Course objective: to learn modern technology for the stereocontrolled assembly of molecules of current biomedical relevance

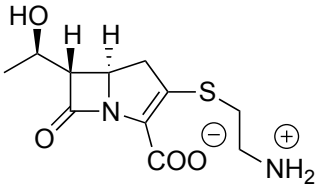
Importance of complex molecules in the pharmaceutical industry of the 21st century

Evolution of the complexity of pharmaceutical molecules during the past century:

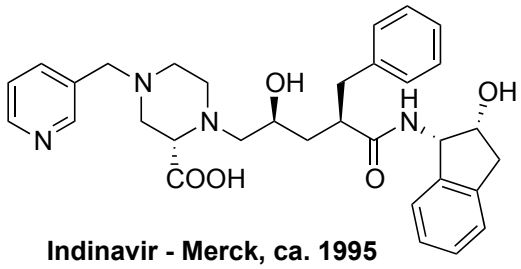
The first 100 years



Aspirin - Bayer, ca. 1880

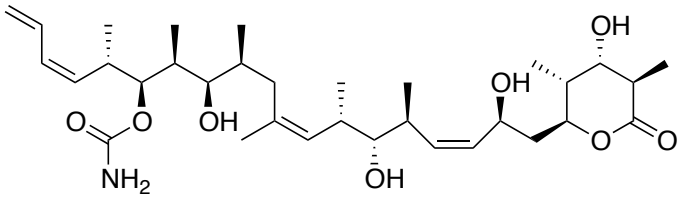


Thienamycin - Merck, ca. 1980

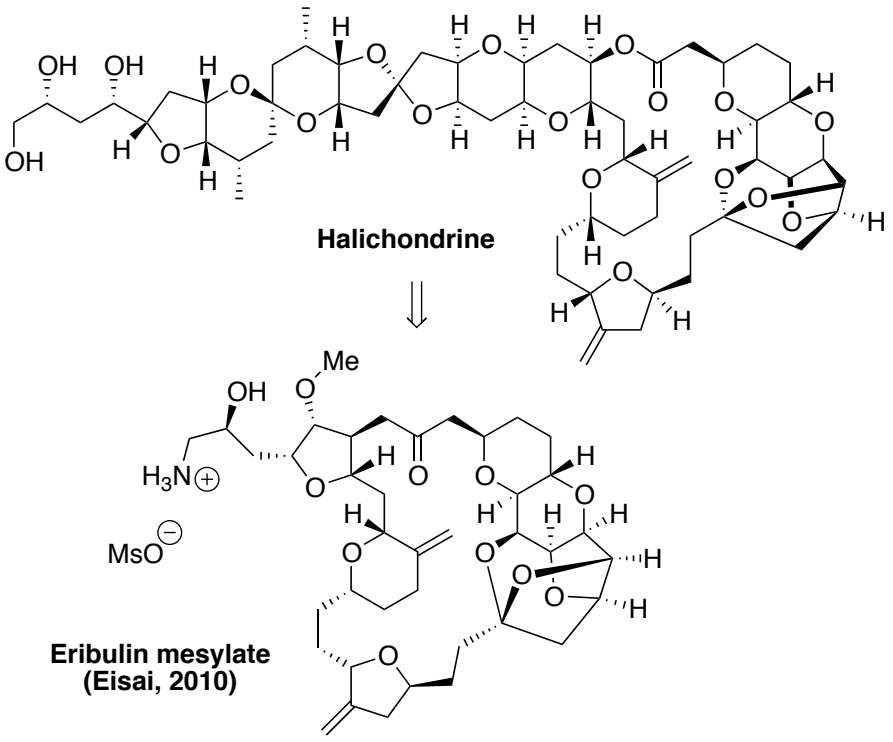


Indinavir - Merck, ca. 1995

The future



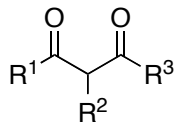
Discodermolide - Novartis, 2004



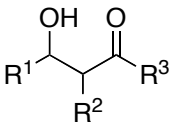
Principle: in order to chart the synthesis of a molecule, however simple or complex it might be, one starts by recognizing the relative position of heteroatomic substituents (N, O, S, halogen, …) around the carbon backbone. This is because the relative position of heteroatoms defines the kind(s) of chemical reactions that one needs to employ to construct the desired molecule (notes of September 11)

Ubiquitous presence of the 1,3-dioxygenated functionality in molecules of biomedical interest

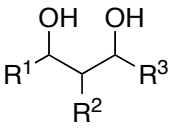
Three types of such 1,3-dioxygenated functionality: 1,3-dicarbonyl, 1,3-hydroxycarbonyl, 1,3-dihydroxy:



1,3-dicarbonyl
(= β-dicarbonyl)
"type A"



1,3-hydoxycarbonyl
(= β-hydroxycarbonyl)
"type B"



1,3-dihydroxy

"type C"

Principle: only a particular configuration of the various stereocenters endows a molecule with the desired bioactivity. Consequently, technology for the assembly of 1,3-dioxygenated functionalities must be:

– diastereocontrolled (it must produce largely / only a given diastereomer of the requisite subunit), and

– enantiocontrolled (it must produce largely / only a given enantiomer of the above diastereomer)

Requirement for effective methods for C-C bond formation in a diastereo– and enantiocontrolled manner

The 1,3-dioxygenated functionality as a logical starting point for the exploration of modern synthetic methodology.