Eclectic enzymes: Easily modified building blocks for drug design

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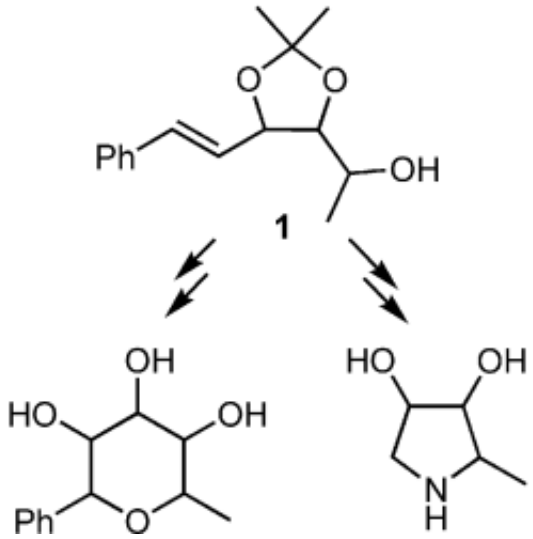

(PhysOrg.com) -- In the pursuit of biologically active compounds, it is often necessary to be able to control the stereochemistry at predefined positions in a molecular skeleton. The search for ways to prepare chiral building blocks with known configuration that also show structural differentiation is important.

Italian scientists working with Elisabetta Brenna have developed a technique to separate individual stereoisomers of building blocks that can be easily integrated into biologically active molecules. As the scientists from Politecnico di Milano, Milano, Italy, report in the

European Journal of Organic Chemistry, their technique relies on the use of enzymes.

The specific activity of a biologically relevant molecule is often dependent on its stereochemistry (i.e., the spatial arrangement of its atoms). However, most compounds showing biological activity have complex structures, making their synthesis difficult. Moreover, compounds with differing stereochemistries can show different activities. Thus, it is sometimes desirable to prepare a range of compounds with the same structural backbone, but having different spatial arrangements of their atoms. The use of configurationally defined building blocks is attractive, but a method to obtain all the stereoisomers of a given building block is thus required.

Brenna and her colleagues have developed a method that allows a mixture of isomers to be differentiated, and it depends on the use of the enzyme lipase PS. The resolution of the stereoisomers relies on the preferential reaction of the enzyme with only one isomer, thereby creating a product mixture containing the desired compound and a mixture of the unreacted isomers. The desired product can be easily separated from the unreacted mixture, which can then be resubjected to the enzyme to undergo further differentiation. In this way, a wide range of building blocks with differing and known stereochemistries can be prepared.

The authors then showed the applicability of their method by incorporating their configurationally defined building blocks into biologically active compounds. Using simple and straightforward organic chemistry transformations, the authors were able to embed their building blocks into two classes of compounds that are of biological interest. Importantly, scientists can now easily examine the biological activities of all the different stereoisomers of a given compound. Thus, the Italian team is well on their way to helping scientists screen a diverse range of

potential drugs that may lead to the treatment, cure, prevention, or diagnosis of diseases.

More information: Elisabetta Brenna, et al., Oxygenated Stereotriads with Definite Absolute Configuration by Lipase-Mediated Kinetic Resolution: De Novo Synthesis of Imino Sugars and 6-Deoxy-C-glycosides, *European Journal of Organic Chemistry*, 2010, No. 23, 4468-4475, dx.doi.org/10.1002/ejoc.201000558

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