PENN CENTER FOR INNOVATION
Empowering Ideas

New tandem epoxidation and oxidation reactions for intermediates in asymmetric organic synthesis

Brief Description
Highly enantio- and diastereoselective synthesis of epoxy alcohols from an aldehyde

Inventor
Patrick J. Walsh, Professor of Chemistry and Alan G. MacDiarmid Term Chair

STATE OF DEVELOPMENT
- Proof-of-principle testing

INTELLECTUAL PROPERTY
USSN 8,236,976

DESIRED PARTNERSHIPS
- License
- Co-development

REFERENCE MEDIA
Kelly A.R. et al. JACS, 2005, 127(42), p. 14668-14674.
Kim H.Y. et al. JACS, 2005, 127(38), p. 13138-13139.
Lurain A.L. et al. J Org Chem, 2005, 70(4), p. 1262-1268.
Lurain A.L. et al. JACS, 2004, 126 (42), p. 13608-13609.

APPLICATIONS
- Versatile intermediates in asymmetric organic synthesis
- Enantiomeric drug synthesis
- Natural product synthesis

LEARN MORE
Sarah Johnson
johnsa@upenn.edu
215-746-7253

Docket #Q3444

Problem
About half of the top-selling pharmaceuticals are single enantiomers, the precursors of which are chiral substances of high optical purity. Controlling the stereochemistry of these materials and creating stereogenic centers allows for the preparation of medicinally relevant target molecules as single enantiomers. There has been a dearth of efficient methods for synthesizing epoxy alcohols, key intermediates in asymmetric organic synthesis. One prominent reaction is the Sharpless asymmetric epoxidation of prochiral allylic alcohols to yield enantio-enriched epoxy alcohols that readily undergo regioselective ring-opening reactions. Epoxy alcohols contain up to three functional groups (olefin, carbinol, and epoxide), for high synthetic potential in generating natural products and pharmaceutical compounds. However, there are chemoselectivity issues in differentiating allylic double bonds when synthesizing allylic epoxy alcohols.

Solution
Researchers in the Walsh lab have developed an enantio- and diastereoselective one-pot synthesis method for acyclic and allylic epoxy alcohols under mild conditions with high yields and in high enantiomeric excess. The method employs an initial asymmetric carbon-carbon bond forming reaction by adding an organozinc or divinylzinc reagent to an aldehyde. The resulting allylic alkoxide intermediate is epoxidized *in situ* in the presence of an oxidant, such as air, and a titanium tetraalkoxide catalyst. Epoxy alcohols with up to three contiguous stereocenters are formed in one pot.

Advantages
- Stereoselective and chemoselective
- One-pot approach for streamlined synthesis
- Circumvents need to prepare and isolate decomposition-prone intermediates
- Compatible with wide range of substrates and catalysts
- Generate up to 3 contiguous stereocenters