THE APPLICATION OF THE SEQUENTIAL BIRCH REDUCTION-ALLYLATION/COPE REARRANGEMENT TO THE ENANTIOSELECTIVE SYNTHESIS OF BIOACTIVE NATURAL PRODUCTS

prof. Wiliam Malachowski

Chemistry Department, Bryn Mayr College, Pennsylvania, USA

The enantioselective synthesis of carbocyclic quaternary stereogenic centers remains an important challenge in organic chemistry and natural product synthesis. We have developed a method for the construction of quaternary stereocenters on a 2-cyclohexen-1-one ring with good to excellent levels of enantioselectivity. The quaternary stereocenter is created through a new synthetic sequence, the Birch-Cope sequence, which involves three reactions: the enantioselective Birch reduction-allylation, enol ether hydrolysis, and the Cope rearrangement. The products of the Birch-Cope sequence are valuable intermediates in the generation of bioactive natural products. The utility of the Birch-Cope sequence products in addressing challenges in natural product synthesis is illustrated with a synthesis of (+)-mesembrine and the first total synthesis of (-)-lycoramine.