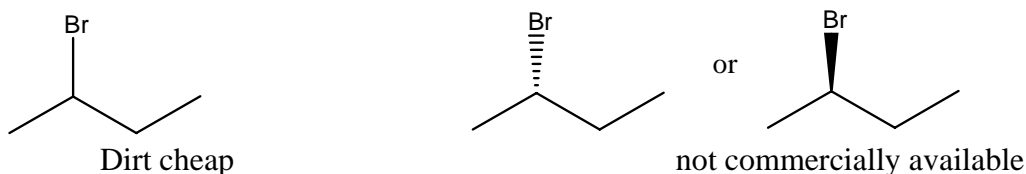


Kinetic Resolution of Challenging Chiral Molecules Using Organocatalysis

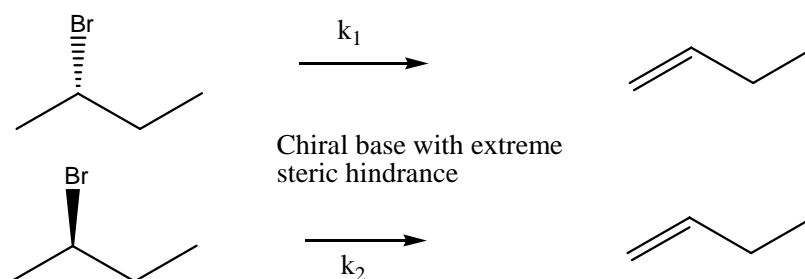
Dr. Kyle Knight

Many important pharmaceuticals are chiral; as are many potential drug candidates. Synthesizing these chiral molecules often requires the use of chiral precursors. Alkyl halides are widely used building blocks in synthesis. They can be readily incorporated into a new structure by simple S_N2 reactions. Indeed the process is known to proceed with inversion, so when the halide substituted carbon reacts, chiral information is preserved.

Remarkably, however, chiral alkyl halides are rarely used in synthesis, because they are not readily available to the chemist. Indeed while racemic 2-bromobutane can be purchased cheaply, the separate enantiomers (R)-2-bromobutane and (S)-2-bromobutane are not commercially available. This lack of availability is a significant hindrance to their use in drug development.



This summer, we will examine the use of kinetic resolution via organocatalysis as a method to obtain the separate enantiomers of simple alkyl halides like 2-bromobutane. This involves exposing the racemic mixture to a chiral reagent that could react with the enantiomers at different rates. If one enantiomer reacts faster, that enantiomer could be selectively removed from the mixture, leaving the other. For instance, in the reaction below, if k_1 is greater than k_2 , the R enantiomer will build up in the reaction mixture.



We will synthesis a series of sterically encumbered chiral bases, and examine them in the above reaction. The extent to which they are selective will be determined by gas chromatography using a chiral column. Students will gain exposure to the techniques of organic synthesis and chemical analysis using NMR and Gas chromatography.