

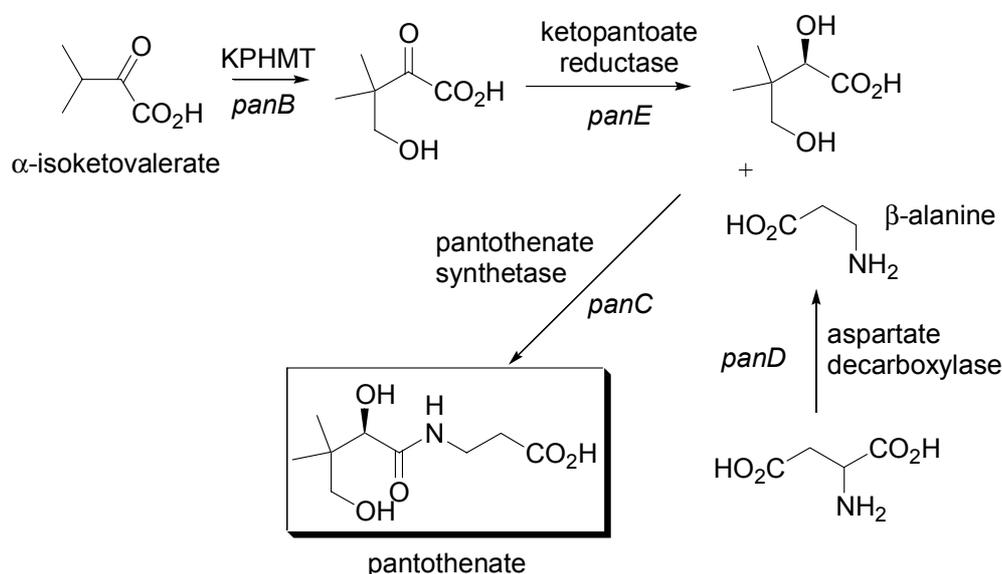
INHIBITION OF PANTOTHENATE SYNTHETASE, AN ENZYME ON THE PANTOTHENATE PATHWAY

Chris Abell^b and Kellie L. Tuck^{a,b}

^aSchool of Chemistry, Monash University, Clayton, Victoria, Australia 3800

^bUniversity Chemical Laboratories, University of Cambridge, Cambridge, UK CB2 1EW.

Pantothenate (otherwise known as Vitamin B5) is a key precursor for the biosynthesis of coenzyme A (CoA) and acyl carrier protein (ACP). Both of these are necessary cofactors for cell growth and are involved in essential biosynthetic pathways. The pantothenate pathway is not present in mammals and consequently represents an exciting target for the development of novel antibiotics and herbicides. The pathway is best understood in *E. coli*, where it comprises four enzymatic reactions.



The biosynthesis of pantothenate (Vitamin B5) in bacteria, yeast and plants.

Pantothenate synthetase is the last enzyme in the pathway, it catalyses the condensation of pantoate and β -alanine in the presence of ATP to give pantothenate. The overall reaction consists of two sequential steps, initial formation of a cofactor-substrate intermediate, followed by subsequent nucleophilic attack on the activated carbonyl by β -alanine. Inhibition of pantothenate synthetase by compounds that mimic the cofactor-substrate intermediate adduct will be discussed.