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The synthesis of potential inhibitors of panthothenate synthetase

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Pantothenate synthetase is the last enzyme in the pantothenate pathway (Fig.1). Pantothenate is biosynthesised in micro-organisms, plants, and fungi, but not in animals, consequently inhibiting pantothenate biosynthesis could offer new drug targets to combat virulent pathogens, for example *Mycobacterium tuberculosis*. Pantothenate synthetase catalyses the ATP-dependent condensation of pantoate and β-alanine, resulting in the formation of pantothenate. It is known that acylsulfamoyl adenosines mimic the pantoyl adenylate intermediate formed during the enzymatic reaction and consequently are potent to good inhibitors.

We have been investigating the role of how variation of the pantoate moiety influences the inhibition of the acylsulfamoyl analogues. Consequently, we have synthesized and tested a series of acylsulfamoyl adenosines in order to explore the role of the pantoate moiety. This talk will describe the synthesis of a range of compounds and their inhibition of pantothenate synthetase.

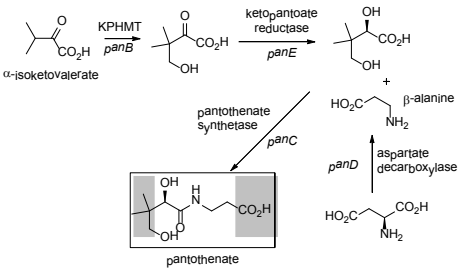

Figure 1: The biosynthesis of pantothenate (Vitamin B5) in bacteria, yeast and plants.

Biography

Kellie L. Tuck completed her Ph.D. studies in 1999 at the age of 24 from the University of Adelaide, Australia. Following this, she worked as a post-doctoral research fellow, at the School of Pharmacy, University of South Australia and University Chemical Laboratories, University of Cambridge. She took up a teaching and research position at Monash University in late 2004. Her research focus is of an interdisciplinary nature and is interested in applying organic chemistry to solve fundamental problems. The results of her research have been published in a total of 43 refereed journal papers.

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