

Synthetic Approach Towards Understanding the Mechanism of Spore Photoproduct Lyase

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In spores of *Bacillus subtilis* the main lesion produced in DNA by UV radiation is a unique thymidine dimer called spore photoproduct (SP, 5-thymidyl-5,6-dihydrothymine). Two forms of SP are proposed to exist in *Bacillus* spores, with the first one being formed between two adjacent thymine residues of the same DNA strand (isomer *R*) and the second produced by dimerization of thymine residues from two different strands (isomer *S*). This DNA mutation is repaired in spores by the enzyme, spore photoproduct lyase (SPL). Preliminary studies have provided evidence that SPL contains an iron-sulfur cluster and requires *S*-adenosylmethionine for catalysis. It is proposed that SPL repairs spore photoproduct through a radical mechanism involving generation of an intermediate adenosyl radical. This intermediate is thought to directly interact with spore photoproduct. However, very little is known about the stereospecificity of this reaction. Herein we present our attempts to synthesize two isomers of 5-thymidyl-5,6-dihydrothymine and test their reactivity as spore photoproduct lyase substrates in order to understand the mechanistic aspects of the SPL reaction.