

P003 Solvent isotope effect on dihydrofolate reductase catalysis
E. Joel Loveridge and Rudolf K. Allemann
*School of Chemistry, Cardiff University, Park Place, Cardiff
CF10 3AT*

Dihydrofolate reductase (DHFR) catalyses hydride transfer from reduced nicotinamide adenine dinucleotide phosphate to dihydrofolate with concomitant protonation. While the hydride transfer step of the reaction has been well described, the protonation step is less well understood. Here, we show that the reactions catalysed by DHFRs from the mesophile *E. coli* and the hyperthermophile *T. maritima* are affected by the isotopic composition of the solvent, providing information on the protonation step of the reaction. Differences between the mechanisms of the reactions catalysed by these two DHFRs are revealed by these data.