

Formation of an MgF_3^- Phosphate Transfer Transition State Analogue in an Enzyme Active Site

Marko Golicnik,¹ Luis F. Olguin,¹ Nicola J. Baxter,² Guoqiang Feng,² G. Michael Blackburn,² Jonathan P. Waltho,² Nicholas H. Williams² and Florian Hollfelder¹

¹ Department of Biochemistry, University of Cambridge, Cambridge CB2 1GA, UK. fh111@cam.ac.uk.

² Centre for Chemical Biology, Department of Chemistry, University of Sheffield, Sheffield S3 7HF, UK.

N.H.Williams@Sheffield.ac.uk

Identifying how enzymes stabilise high-energy species along the reaction pathway is central to explaining their enormous rate acceleration. β -Phosphoglucomutase (β -PGM) catalyses the isomerisation of β -glucose-1-phosphate to β -glucose-6-phosphate. Using ^{19}F -NMR and kinetic analysis, we report how MgF_3^- -complex forms in which MgF_3^- mimics the transferring PO_3^- moiety. We resolve its formation by steady-state and pre-steady state kinetics and propose a molecular mechanism for fluoride inhibition of β -phosphoglucomutase.

References:

- Baxter, N. J.; Olguin, L. F.; Golicnik, M.; Feng, G.; Hounslow, A. M.; Bermel, W.; Blackburn, G. M.; Hollfelder, F.; Waltho, J. P.; Williams, N. H. *Proc Natl Acad Sci U S A* **2006**, *103*, 14732-7.
- Baxter, N. J.; Blackburn, G. M.; Marston, J. P.; Hounslow, A. M.; Cliff, M. J.; Bermel, W.; Williams, N. H.; Hollfelder, F.; Wemmer, D. E.; Waltho, J. P. *J Am Chem Soc* **2008**, *130*, 3952-8.