

P022 Oxacarbenium ion intermediates in enzyme catalyzed glycoside hydrolysis

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The existence of oxacarbenium ion intermediates in enzyme catalyzed glycoside hydrolysis has been of continuing interest since the determination of the structure of hen egg-white lysozyme and the contrasting mechanistic proposals of Phillips and Koshland.

Typically, mechanistic studies probing stepwise and concerted pathways of glycoside hydrolysis have relied upon the use of kinetic isotope effects and their interpretation using small computational models. In the case of human O-GlcNAcase (an enzyme belonging to glycosyl hydrolase family 84) multiple linear free energy relationship studies (Brønsted and Taft type) provide a complementary approach to kinetic isotope effects based studies. The results of these studies are best explained by a stepwise mechanism involving nucleophilic preassociation ($D_N^* A_N$). These findings are supported by QM/MM free energy simulations (one dimensional and two dimensional potentials of the mean force) of the mechanism of *Bacteriodes thetaiotaomicron* β -hexosaminidase, a homologous enzyme also belonging to glycosyl hydrolase family 84.