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X-Ray Structure of a Bound Phosphonate Transition State Analog and Enantioselectivity of *Candida rugosa* lipase toward Chiral Carboxylic Acids

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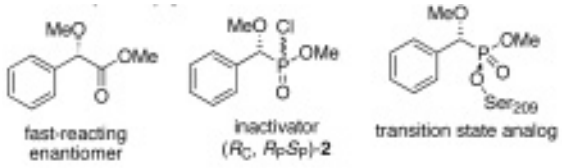
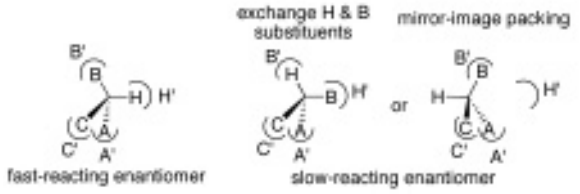
Keywords: protein-ligand complexes, enzyme catalysis, chirality

Candida rugosa lipase (CRL) resolves chiral aryloxy- and arylpropionic acids with moderate to high enantioselectivity [1]. To understand how CRL distinguishes between enantiomers, we determined the X-ray crystal structure of a transition state analog for a typical enantiomer of a chiral carboxylic acid ester, methyl α-methoxyphenyl acetate, **1**, covalently linked to CRL. Purified CRL shows moderate enantioselectivity (E = 23) toward this chiral acid favoring the (*S*)-enantiomer. To prepare a transition state analog that mimics reaction of the fast reacting enantiomer, we prepared inactivator (R_C,$R_P$$S_P$)-**2**. An X-ray crystal structure of CRL containing the covalently linked transition state analog shows the phenyl ring in the hydrophobic tunnel of the lipase, as proposed previously based on molecular modeling [1]. Phe344 and Ph415 crowd the region near the substrate stereocenter, suggesting that shape of the active site prevents binding the slow-reacting enantiomer in a catalytically productive orientation.



Previous x-ray crystal structures of enantiomers bound to enzymes show that their relative orientation is either an exchange of two substituent positions or, more commonly, a mirror image orientation [2]. Modeling will test both of these possibilities for the slow enantiomer of **1**.



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SdsA1 from *P. aeruginosa*, defines a new mechanistic class of sulfatases

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Keywords: sulfatases, metalloenzymes, mechanisms

Pseudomonas aeruginosa exhibits a remarkable metabolic versatility allowing it to occupy a multitude of ecological niches. Strikingly, it is able to degrade and utilize biocidic sodium dodecyl-sulfate (SDS), the detergent of most commercial personal hygiene products. We identify SdsA1 of *P. aeruginosa* as a secreted SDS-hydrolase that allows the bacterium to utilize primary sulfates such as SDS as sole carbon or sulfur source. The crystal structure of SdsA1 reveals three distinct domains. The N-terminal catalytic domain with a binuclear Zn^{2+} cluster is a new member of the metallo-β-lactamase fold family, the central dimerization domain ensures resistance to high concentrations of SDS, while the C-terminal domain provides a hydrophobic groove, presumably to recruit long aliphatic substrates. Crystal structures of apo-SdsA1, and complexes with a substrate-analog and products, indicate a novel enzymatic mechanism involving a water molecule indirectly activated by the Zn^{2+} cluster.